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DUPLICATION OF THE BOWEL: CASE REPORT

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A 3-year-old male Bantu child was admitted to the Baragwanath Hospital on 24 February 1954 with a provisional diagnosis of bilateral congenital cystic disease of the kidneys. The history, as obtained from the mother and corroborated by the doctor who sent the case in, was that the child was born with a large abdominal mass. This mass was never constant in size, but had fluctuated and on occasion had even disappeared. The patient had once been admitted to another hospital as a case of tuberculous peritonitis and had been treated with streptomycin. The swelling had subsided with this treatment. Before admission to Baragwanath Hospital the mass had increased to a size much larger than seen on any previous occasion.

After the child had been in the ward for a few days, the mass, which had presented the appearance seen in Fig. 1, suddenly diminished in size and almost disappeared. As far as could be ascertained this was not accompanied by polyuria or diarrhoea. Intravenous pyelography and straight X-ray examination of the abdomen at this stage showed no abnormality.

The child was sent to the convalescent ward for observation, and after he had been there for about 10 days, he became acutely ill, and vomited, and the abdominal mass was found to have grown fairly rapidly to its former size.

I was called to see the child at this stage. On examination, a very large dumb-bell shaped mass was felt at the level of the umbilicus stretching transversely across the abdomen. The central constriction was due to the vertebral column. The mass was cystic in nature, extremely heavy, and fairly mobile. It was dull to percussion. Having previously been painless, it was now tender, and the child tended to assume a knee-elbow position which apparently relieved the pain. Nothing else significant was found except an undescended left testis.

The child's condition deteriorated, the mass became extremely tender and the child developed signs of an acute intestinal obstruction. On 17 March 1954 it was decided to operate.

A transverse supra-umbilical incision was made. A large cystic mass was seen, which was lying transversely across the abdomen and which was adherent to the parietal peritoneum in the flanks. After the adhesions were freed the cyst was found to have a pedicle, which had been twisted through an angle of 90°. After the pedicle was untwisted this large elongated mass lay perpendicularly in the abdomen, swinging from a fairly small pedicle which was found to be continuous, at its origin, with the mesentery of the terminal ileum. There were several large vessels in the pedicle. The pedicle was clamped, ligated, and divided, and the cyst removed.

On examination (Fig. 3) the cyst was found to be completely closed at both ends. It measured 10 inches long by 3 inches across. Both ends were very much narrower than the rest of the mass, and at the point of narrowing the ends were acutely flexed on the main tumour. The cyst was found to contain 1,200 c.c. of straw-coloured fluid. A small amount of freshly shed blood was found adherent to the wall of the cyst at its mesenteric (or pedicle) portion. Examination of the fluid showed a protein content of 3 g. per 100 c.c. There was no bacterial growth on cultivation.

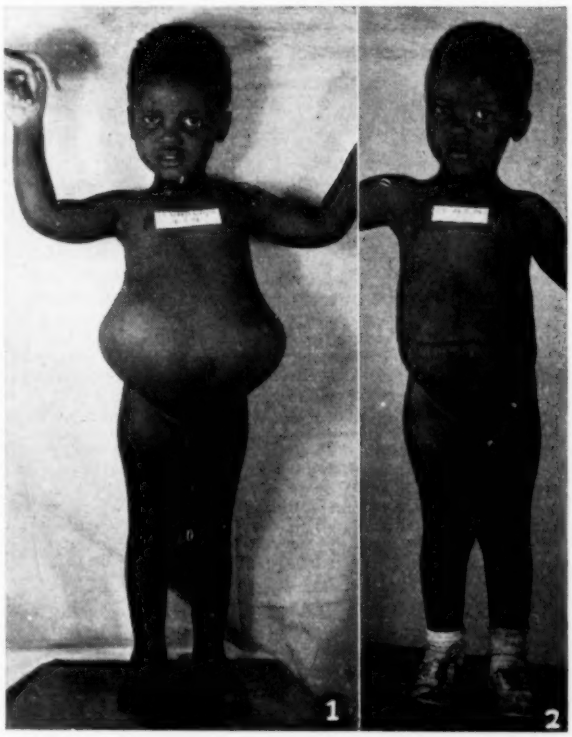

Fig. 1. Photograph of child taken before operation.
Fig. 2. Photograph of child after operation.

Histological section was reported on as follows by Dr. B. Grobelaar of the South African Institute of Medical Research:

'Section of the large cyst shows the wall to consist of an inner circular and outer longitudinal muscle-layer, covered by a layer

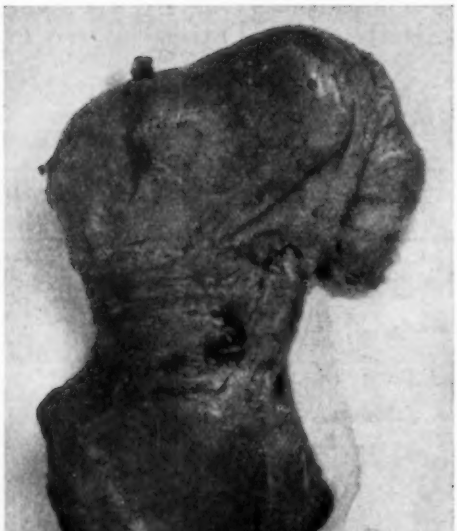

Fig. 3. Photograph of specimen removed from patient.

of mesothelial cells resting on loose connective tissue. The cyst is lined by a mucous membrane of columnar cells. In some areas the mucous membrane is destroyed, the wall in these parts being lined by loose connective tissue.

'Sections of the smaller terminal portions of the cyst have a similar structure, being lined by a mucous membrane consisting of numerous villi covered by tall mucin-secreting columnar cells.

'The histological features are identical with those of the wall of normal small intestine.'

The patient made an uninterrupted recovery. When he was seen some 10 weeks after the operation, the abdomen was normal in size and the previously atonic abdominal musculature had recovered (Fig. 2).

DISCUSSION

Duplication of the bowel has been described under various names, e.g. enterogenous cyst, ileum duplex, giant diverticulum, inclusion cyst, gastric-thoracic cyst.[1] They are very rare and are almost always situated close to the ileocaecal region.[2] They may, however, present in other situations, e.g. thorax, base of tongue, and different parts of the abdomen, and are very variable in size and shape.

Interesting features of the above case were:

1. The amount of fluid present in the cyst (1,200 c.c., i.e. practically equivalent to the total circulating volume).

2. The cyst varied in size, suggesting a partial or intermittent communication with the bowel. At operation no such communication was found, and no air or obvious intestinal content was found in the cyst. Possibly the fluid may have escaped *via* the venous return after absorption through the mucosa. In Gross's series about 20% showed a communication with the bowel.[1]

Several theories have been put forward to explain the origin of duplications. It has been shown that diverticula occur normally in the foetus of pigs, rabbits, cats, sheep and humans.[3] These normally regress but one or more may persist and sequestrate off. Bremer[4] states that duplications arise when the normally solid stage of the bowel becomes hollowed in the foetus. During this stage multiple vacuoles appear which later coalesce to form a hollow tube. Failure to coalesce may give rise to atresias. It is possible that one or more of these vacuoles may not communicate with the rest and may thereby form a hollow duplication on its own, with all the histological constituents of normal bowel, and in all probability having a communication with the main tube. Du Toit[5] has reported a case with a free communication, found incidentally at operation.

SUMMARY

A case of duplication of the bowel is described in a child aged 3. A feature of the case was that the cyst was capable, periodically, of emptying itself of its contents. Some of the theories of etiology of duplication are discussed.

I should like to thank Dr. J. Allen, Superintendent of Baragwanath Hospital, for permission to publish this case; also Dr. S. Wayburne for his assistance with the case and for his photography.

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OFFICIAL ANNOUNCEMENT : AMPTELIKE AANKONDIGINGS

TARIFF FOR MEDICAL AID SOCIETIES

Confinement Fees: In conjunction with the Executive of the Central Committee for Contract Practice the representatives of approved medical aid societies agreed to an increase in the fee for confinements (item B. 5 in the Tariff Book) from £12 12s. 0d. to £15 15s. 0d. This increase will become effective from 1 January 1957.

L. M. Marchand
Associate Secretary

Medical House
Cape Town
5 December 1956

TARIEF VIR MEDIESE HULPVERENIGINGS

Bevallingskoste: In oorleg met die dagbestuur van die Komitee i.v.m. Kontrakpraktyk het die verteenwoordigers van erkende mediese hulpverenigings ooreengekom dat die gelde vir kraamgevalle (item B. 5 in die tariefboek) van £12 12s. 0d. tot £15 15s. 0d. verhoog word. Hierdie verhoging tree in werking met ingang 1 Januarie 1957.

L. M. Marchand
Medesekretaris

Mediese Huis
Kaapstad
5 Desember 1956

South African Medical Journal

Suid-Afrikaanse Tydskrif vir Geneeskunde

EDITORIAL

TREATMENT OF INTESTINAL AMOEBIASIS

Assessment of results of treatment of intestinal amoebiasis is complicated by the difficulty of conducting adequate follow-up studies, particularly in backward communities, by controversy on what constitutes pathogenicity in the cystic and vegetative forms of amoebae, and by the difficulty in deciding on clinical grounds between true relapse and post-dysenteric colonic syndromes.

It is still uncertain what is the best form of treatment of the disease in spite of much research in recent years and the development of new amoebicidal drugs.

In 1912, Rogers, who had used ipecacuanha with fair success, popularized the use of emetine, its active principle, in the treatment of amoebiasis, and this drug and its iodine compounds (emetine-bismuth-iodide, auremetin, etc.) together with the trivalent arsenicals (stovarsol, carbasone, milibis) and the iodo-oxyquinolines (chiniofon, vioform, diodoquin) were the sheet-anchor in the treatment of the disease and its complications for over 30 years.

There was some dissatisfaction with the results of this treatment, partly because of an exaggerated fear of the toxic effects of emetine and the arsenical compounds. Emetine-bismuth-iodide gave uncertain results, but it is now well known that the method formerly used of dispensing the substance in keratin-coated tablets permitted their passage through the bowel unabsorbed.

In South Africa, Armstrong *et al.*,[1] working in Natal, where a particularly severe form of amoebiasis is frequent in the Bantu population, carried out an impressive series of researches into the efficacy of various drugs, and found that as far as immediate control of the disease was concerned, a combination of emetine and diodoquin was effective in itself, and that the effects were enhanced by the addition of sulphasuccidin and penicillin. No information on relapse rates were available. EBI by mouth was as effective as emetine by injection.

During the last half-dozen years the amoebicidal value of the antibiotics has been receiving increasing attention. Most *et al.*,[2] in Korea, and the Natal group of workers, Elsdon-Dew, Armstrong and Wilmot,[3] obtained encouraging results with oxytetracycline (terramycin).

VAN DIE REDAKSIE

BEHANDELING VAN INGEWANDSAMEBIASE

Berekening van resultate van die behandeling van ingewandsamebiase word ingewikkeld gemaak deur die moeilikheid om geskikte opvolgingsstudies uit te voer, veral in agterlike gemeenskappe, deur geskil oor wat patogeniteit by die sistiese en vegetatiewe vorms van amebes uitmaak, en deur die moeilikheid om op kliniese gronde tussen ware hervatting en na-disenteriese sindrome van die dikderm te besluit.

Ten spyte van baie navorsingswerk wat gedurende die afgelope jare gedoen is en die ontwikkeling van nuwe amebisidale geneesmiddels, is dit nog onseker wat die beste vorm van behandeling van die siekte is.

In 1912 het Rogers, wat ipekakuanha met 'n mate van sukses gebruik het, die gebruik van emetien, sy aktiewe bestanddeel, gewild gemaak by die behandeling van amebiase, en hierdie geneesmiddel en sy jodiumverbindings (emetien-bismut-jodied, ouremetien, ens.) tesame met die driewaardige organiese arseenverbindings (stovarsol, karbasoon, milibis) en die jodo-oksichinoliene (chiniofon, vioform, diodochin), was vir langer as 30 jaar die nood-anker by die behandeling van die siekte en sy komplikasies.

Daar was 'n mate van ontevredenheid met die resultate van hierdie behandeling, gedeeltelik weens 'n oordrewe vrees vir die toksiese uitwerkings van emetien en die arseenhoudende verbindings. Resultate met emetien-bismut-jodied was onseker, maar dit is nou welbekend dat die metode wat voorheen gebruik is om die stof in keratien-oorgetrekte tablette op te maak, toegelaat het dat hulle ongeabsorbeerd deur die ingewande gaan.

In Suid-Afrika het Armstrong *et al.*,[1] terwyl hulle besig was met navorsing in Natal waar 'n besonder strawwe vorm van amebiase dikwels by die Bantoebevolking voorkom, 'n indrukwekkende reeks navorsings in die doeltreffendheid van verskeie geneesmiddels uitgevoer en gevind dat, sover dit onmiddellike beheer van die siekte betref, 'n verbinding van emetien en diodochin of sigself doeltreffend was, en dat die uitwerkings met die byvoeging van sulfasuksidien en penisillien verhoog was. Daar was geen inligting aangaande die hervattingssyfers beskikbaar nie. Mondelikse toediening van EBI was net so doeltreffend soos die toediening van emetien deur inspuiting.

Gedurende die afgelope halfdosyn jare het die amebisidale waarde van die antibiotika tonemende aandag geniet. Most *et al.*[2] in Korea, en die Natalse groep navorsers Elsdon-Dew, Armstrong en Wilmot,[3] het bemoedigende resultate met oksitetrasiklien (terra-

The usefulness of these drugs should be assessed in the light of their high cost and the danger of producing resistant staphylococci and other bacteria, and by the uncertainty about relapse rates after this form of treatment.

In a recent symposium of the Royal Society of Tropical Medicine and Hygiene, Woodruff *et al.*[4] described the results of therapeutic trials carried out in London on a large series of patients, who were drawn from most parts of the world, mainly from India and tropical Africa, to compare the effects of some of the newer anti-amoebic substances and the antibiotics, with those of EBI used alone or in combination with other drugs. Their conclusions, drawn from a study of 417 patients, are that EBI is the most satisfactory drug available at present. Relapse rates with chloramphenicol and chlortetracycline (aureomycin) were high, but oxytetracycline (terramycin) gave good results. Toxic effects, including dermatitis and albuminuria, occurred with the use of fumagillin. Treatment with glaucarubin, camoform and dichloracethydroxymethylanilide had at best no advantages over the older drugs.

On grounds of efficacy, ease of administration and cost, emetine appears to have retained pride of place as an amoebicide for routine use, in spite of efforts to replace it by newer drugs. In South Africa, certainly in European patients, in whom the disease tends to be less severe than in the Bantu, available evidence points to the following routine as being the best standard form of treatment. In acute cases a daily injection of 1 gr. of emetine is given for 3 days to produce rapid control of the symptoms, followed by an enteric-coated 3-gr. tablet of EBI nightly for 10 days together with a sedative to overcome nausea, which generally appears after 2 or 3 days. This is followed by 10 tablets of diodoquin daily for 20 days. Antibiotics should be reserved for patients who relapse after the course of EBI.

In the Bantu the disease often assumes a fulminating form, with gross ulceration of the colon and rectum and associated sepsis, and the combination of antibiotic drugs with the treatment already outlined will enhance the chances of immediate control and permanent cure.

As regards hepatic complications, the anti-malarial substance, chloroquine, used in combination with parenterally administered emetine, is a specific antidote against amoebiasis of the liver, but it has no apparent effect on intestinal infections.

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misien) gekry. Die bruikbaarheid van hierdie geneesmiddels behoort bereken te word in die lig van hulle hoë koste en die gevaar dat weerstandbiedende stafilokokke en ander bakterieë voortgebring mag word, en deur die onsekerheid aangaande die hervattingssyfer ná hierdie vorm van behandeling.

In 'n onlangse simposium van die Royal Society of Tropical Medicine and Hygiene, het Woodruff *et al.*[4] die resultate van terapeutiese proefnemings beskryf wat in Londen op 'n groot reeks pasiënte uitgevoer is, wat van byna al die dele van die wêreld, hoofsaaklik van Indië en tropiese Afrika, verkry was, om die uitwerkings van sommige van die nuwer anti-amebiese stowwe en die antibiotika te vergelyk met dié van EBI wat alleen of in verbinding met ander geneesmiddels gebruik is. Die gevolgtrekkings waartoe hulle gekom het na 'n studie van 417 pasiënte, is dat EBI die mees bevredigende geneesmiddel is wat op die oomblik beskikbaar is. Hervattingssyfers met chlooramfenikol en chloortetrasiklien (oureomisien) was hoog, maar oksitetrasiklien (terramisien) het goeie resultate gelewer. Toksiese uitwerkings, insluitende huidontsteking en albuminurie, het by die gebruik van fumagillien voorgekom. Op sy beste het behandeling met gloukarubien, kamoform en dichlooraset-hidroksiemetielanilied geen voorsprong op die ouer geneesmiddels gehad nie.

Op grond van doeltreffendheid, gemak van aanwending, en koste, skyn dit of emetien, ten spyte van pogings om dit met nuwer geneesmiddels te vervang, sy ereplek as 'n amebisied vir roetiene gebruik behou het. Beskikbare bewys vestig die aandag daarop dat in Suid-Afrika, sekerlik by blanke pasiënte by wie die siekte geneig is om minder straf te wees as by die Bantoe, die volgende roetine die beste standaard vorm van behandeling is. By akute gevalle word 'n daaglikse inspuiting van 1 gr. emetien vir 3 dae gegee om 'n spoedige beheer oor die simptome te kry, gevolg deur 'n 3-gr. dermpil van EBI elke aand vir 10 dae, tesame met 'n kalmeermiddel om mislikheid, wat gewoonlik na 2 of 3 dae voorkom, te bowe te kom. Dit word gevolg deur 10 diodochin-pille daagliks vir 20 dae. Antibiotika behoort gereserveer te word vir pasiënte by wie die siekte ná die EBI-reeks hervat.

By die Bantoe neem die siekte dikwels 'n uitbarstende vorm aan met ernstige ulserering van die dikderm en nersderm, en geassosieerde sepsis, en die kombinasie van antibiotiese geneesmiddels met die behandeling, waarvan die hoofpunte alreeds beskrywe is, sal die kanse van onmiddellike beheer en permanente kuur verhoog.

Wat komplikasies van die lewer betref, is chloorochien, die anti-malaria stof, wat saam met parenteraal toegediende emetien gebruik word, 'n spesifieke teengif teen amebiase van die lewer, maar dit het geen sigbare uitwerking op infeksies van die ingewande nie.

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CAESAR'S WIFE

A doctor's reputation, like that of a woman, has been compared with a mirror—the merest breath clouds it. It is unnecessary that a doctor do anything illegal, unethical or immoral, the very suggestion that he might ever be capable of doing these things is sufficient to besmirch this very delicate flower.

The doctor, for this reason, has always been in a very vulnerable position. Quite apart from his professional activities, which he is obliged to carry out in a strictly ethical way, his lay activities are constantly in the public eye and the least comment on these is often fatal to his professional status. It has been said that in business there is no such thing as bad publicity—so far as a doctor's business is concerned, there is no such thing as good publicity. All of us who have practised our profession are aware of these pitfalls and beware of them. There is a fairly strict selection of the type of man who is going to become a doctor, which is made early on in his academic career, and this selection operates all through the long years of his study and apprenticeship. So it should be, and long may it continue so to be.

But the very vulnerability of the doctor's position makes it incumbent on all intelligent men to consider very carefully the consequences that may arise out of foolish, malicious or merely idle chatter. More than anyone else, doctors should consider this position and be most careful about making their colleagues the subjects of tea-table conversation or bar-room talk. The damning with faint praise and the slightest suggestion of professional or personal lack of complete integrity should all be abjured and while the general public cannot be expected to be aware of all the nuances and implications of light talk, more must be expected from medical men; it is one of the restrictions to which doctors are subject and a restriction moreover which we should be proud to preserve.

THE DIAGNOSIS OF EARLY GENITAL CANCER AND OTHER ABNORMALITIES BY CYTOLOGY

A PILOT SURVEY

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and

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The detection and treatment of early cancer is a subject that is constantly receiving the active attention of workers throughout the world. In recent years many notable advances in technique have been made and, whilst it is too early to assess the effectiveness of the methods applied, some measure of the attained success can be determined in at least one direction—the detection of early carcinoma of the female genitalia by exfoliative cytology. Any method offering even a modicum of hope in this disease is deserving of the fullest application. The magnitude of cancer incidence and mortality throughout the world demands support for research projects probing towards knowledge of the aetiology, possible epidemiology and sound treatment of this dreaded disease. Charcot said: 'To learn how to treat disease, one must learn how to recognize it. The diagnosis is the best trump in the scheme of treatment'.

Dorn[1] has estimated that approximately 300,000 new cases of cancer are detected in the United States each year, and, from his own studies, found that 34% of patients die within one year after the diagnosis of cancer is made. In unselected cancer cases the survival period is considerably less than the arbitrary 5-year figure. Statistics reported by Papanicolaou and Traut[2] show that 32,000 women die annually in the United States from carcinoma of the genital tract and that, of these deaths, 26,000 may be attributed to uterine cancer.

The need for urgency in diagnosing early cancer is readily appreciated when it is considered that 60 out of every 100 women suffering from malignant genital neoplasms present themselves too late for adequate treatment. It is before leucorrhoea, blood-stained vaginal discharge and contact bleeding are present that the pre-invasive carcinomatous lesion and the earliest invasive cancer must be diagnosed if prevention is to be ensured or the best, i.e. the earliest, possible treatment is to be instituted. Early diagnosis and immediate treatment, therefore, still carry with them the best possible prognosis.

The study of exfoliated material from the genital tract is a valuable diagnostic aid that has been developed over the past 15 years. By this method malignant cells may be detected in secretions obtained from various levels in the genital tract. The presence of cancer cells in secretions obtained from the cervix and vagina is of inestimable value in the diagnosis of early carcinoma of the cervix and also of the uterine body. It should be emphasized, however, that the examination of exfoliated material by the smear technique should not be considered a substitute for biopsy or curettage

but should be accepted as a preliminary method in the diagnosis of early carcimoma. The value of the exfoliative cytological smear in the practice of gynaecology is established. The results obtained will serve to lend additional weight to Traut's statement[3] that the vaginal smear represents the most important single diagnostic test in the armamentarium of the gynaecologist and to Ayre's statement[4] that 'the cytology smear and scraping which may today be placed in the hands of every medical practitioner will go a long way towards curbing mortality in the common and deadly uterine cancer'.

DEVELOPMENT OF SMEAR DIAGNOSIS

The study of the structure of individual cells as an aid to clinical diagnosis is well over a hundred years old. As far back as 1853 Donaldson[5] described the cells seen in 'tumour juice'. Beale[6] followed in 1860 by describing cancer cells seen in sputum from a case of carcinoma of the pharynx. Dudgeon and Wrigley[7] reported in 1935 that in their examination of pulmonary secretions for evidence of malignancy they found cells which were of diagnostic value. Bamforth[8] (1946) in his work on sputa and pleural fluids achieved a high degree of accuracy in diagnosing pulmonary cancer by determining the presence of malignant cells in these media.

It was in 1928 that exfoliative cytology was first used as a means of diagnosis in gynaecology; in this year Papanicolaou[9] reported finding cancer cells in the vaginal secretions of women suffering from uterine carcinoma. The full realization of the true significance of this report was long delayed and, as a result, development of this study was somewhat slow. Papanicolaou and Traut,[2] during the last war, viz. in 1941, having made further technical advances, suggested the possible application of the vaginal smear to the diagnosis of carcinoma of the female genitalia. These authors proved that specific malignant cells could, with a high degree of accuracy, be found in smears from women with known cancer. It is to these workers that tribute must be paid for the development of the technique which enabled this method to be used as a routine procedure, thus opening up a new vista in the early diagnosis of cancer and giving impetus to further investigation into this problem. Confirmation of the accuracy and value of exfoliative cytology as an aid to the diagnosis of malignancy was soon forthcoming.

Meigs, Graham and their co-workers[10] were foremost in confirming the technique for the identification of malignant cells in secretions of the cervix and vagina. Ayre,[11] Jones and Neustaedter,[12] Gates and Warren[13] and others[14,15,16] published results which collectively represented many thousands of investigations and adequately demonstrated that the method might be used as an indicator of the presence of malignancy with accuracy comparable to that shown by histological examination of biopsy material. Fremont-Smith, Graham and Meigs[17] reported a number of instances in which examination of the cervical or vaginal smears revealed the presence of cancer cells in cases where biopsy of the cervix had, in the first instance, failed to demonstrate malignancy.

Ayre, in his earlier work, had aspirated the secretion direct from the external os of the cervix and by this method had found a greater concentration of cancer cells in the material for study. In a few cases a small number of cells of the cancer type were found in the absence of lesions of a suspicious nature. This led to the development by Ayre[18] of the wooden spatula

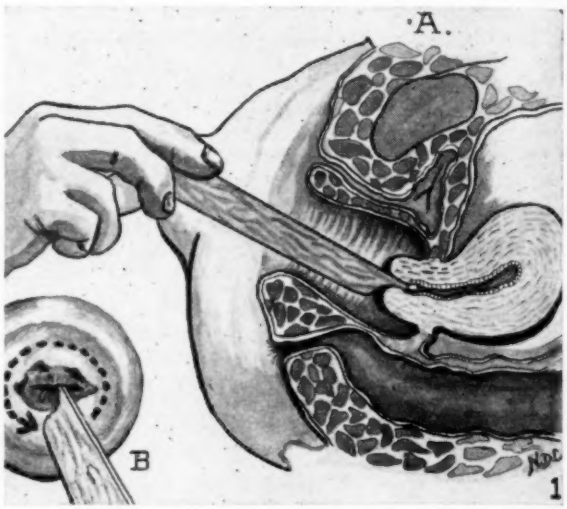

Fig. 1. Collection of secretion for smears by cervical scraping. A. Spatula cut to shape of cervix is introduced into the cervical canal for collection of cervical smear. B. The spatula is rotated through the entire circumference to obtain material from the cervix.

cut to fit the cervix and which, when rotated, would scrape the squamo-columnar junction throughout its entire circumference (Fig. 1). This method has the undoubted advantage of producing smears with a high cell-content and which contain cells from the squamo-columnar junction—a site where, it is stated, carcinoma frequently originates. Its disadvantage is that the sample of cells obtained is not representative of the whole genital tract.

Papanicolaou's method[19] of obtaining material for study from the posterior fornix is based on the fact that the mucous membrane of the female genital canal is in a continual state of exfoliating cells into its lumen. Any tumour present also exfoliates cells, so that this pool of vaginal secretion may contain the exfoliated cells from the normal mucosa in addition to that from the neoplastic area. To obtain the material Papanicolaou makes use of a slightly-curved glass pipette, 15 cm. long, fitted with a rubber bulb. The secretion is aspirated from the posterior fornix of the vagina (Fig. 2).

Many other methods of obtaining material have been suggested. Gladstone [20,21] devised a simplified method for detaching living cells directly from the suspect area in a suitable form for embedding in paraffin wax. The technique consists essentially of gently rubbing the suspected area with a small sponge. Cells and fluid exuded from the tissue are absorbed by the sponge,

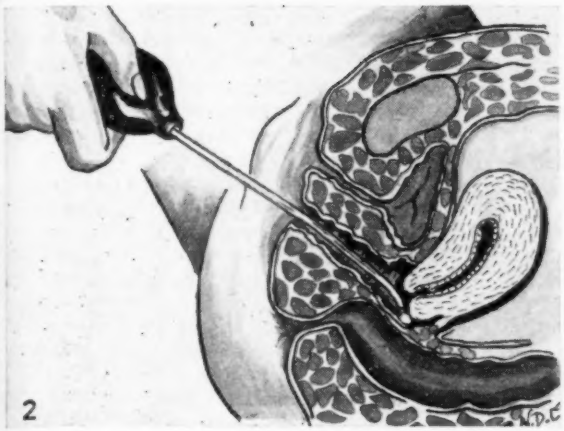

Fig. 2. Vaginal smear secretion is aspirated from the posterior fornix of the vagina.

which is then placed into a histological fixative; the sponge and its absorbed content is then treated as a biopsy specimen, being embedded in paraffin wax, cut on a microtome, and stained by haematoxylin and eosin. Other methods include the use of special metal cannulae, and cotton-wool swabs on wooden applicators. Where the vaginal secretion is scanty it has been suggested that a specimen be obtained by irrigating the vaginal canal with saline solution containing 10% alcohol; the ensuing 'washings' are then centrifuged and the sediment spread on albumized slides. Of the many methods suggested for obtaining exfoliated material, Papanicolaou's method and that advocated by Ayre remain those of general acceptance. A combination of both methods, in our experience, approaches the ideal.

WORK AT GROOTE SCHUUR HOSPITAL

For the past 18 months the study of exfoliated material for the presence of malignancy has been part of the investigation into carcinoma of the female genitalia which has been undertaken at a specialized clinic in the Gynaecological Out-Patients Department of Groote Schuur Hospital. A total of 2,150 smears from 1,050 patients have been examined for malignancy. Statistical analysis of the results of the study of these smears is to be carried out when adequate 'follow-up' of the patients' case histories has been completed. Additional to the cases investigated for evidence of malignancy, a large number of smears were examined from patients suspected of oestrogenic dysfunction, and a number for chromosomal sexing.

Early in the series the value of the smear method of examination was manifest in directions other than those for evidence of malignancy. *Trichomonas vaginalis* (Fig. 3) and *Monilia* (Fig. 4), the 2 commonest parasites of the female genital tract, could, after staining by the Papanicolaou series of stains, be demonstrated with a clarity rarely achieved by other staining methods. A considerable number of smears revealed the presence

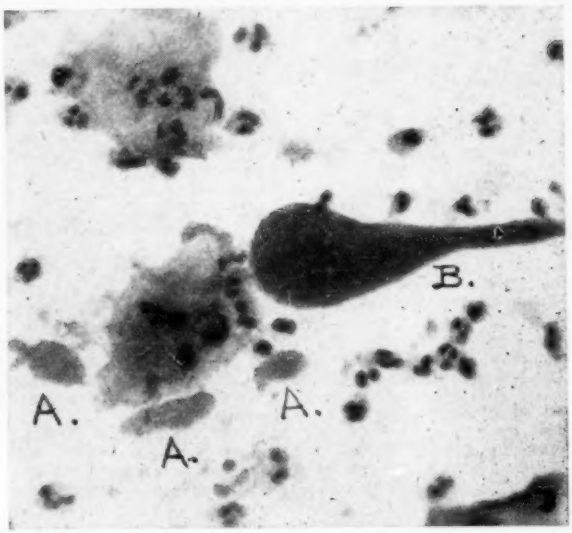

Fig. 3. Trichomonads (A) in vaginal smear with benign atypical cell (B) often seen in trichomonad infestation. Stained by Papanicolaou's method.

of *Trichomonas vaginalis*, and in many of these cases the morphological characteristics of the cells retained their normality. Ayre,[22] also noting this feature, states: 'It is perhaps of significance that these cells show normal morphologic characteristics rather than those of inflammatory hyperplasia, commonly associated with the clinical and cell finding of trichomoniasis. The inference is that this type of trichomonad may be of low irritative type so far as this individual is concerned.

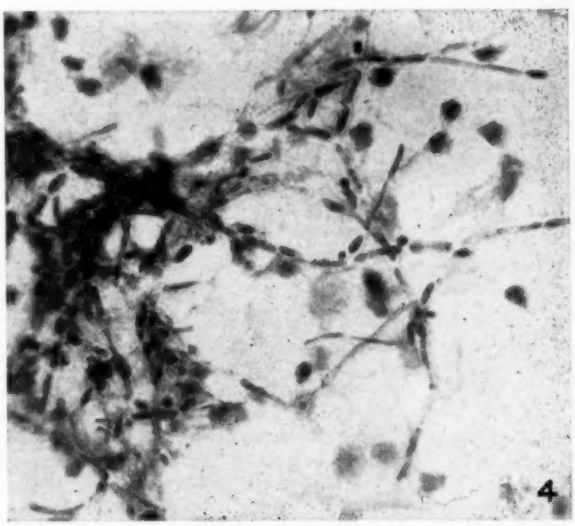

Fig. 4. Monilia obtained through vaginal smear. Demonstrated by Papanicolaou's stain.

In view of the frequent evidence of trichomonads in smears of asymptomatic women, it is our belief that this infestation is considerably more general than commonly believed'.

Numerous methods have been suggested for staining the smears. Yue *et al.*[23]; reported that exfoliated cells obtained from the vagina were readily stained by a solution of silver carbonate prepared according to the formula used by Del Rio-Hortega[24] for the impregnation of microglia. They stated that chromatin material was particularly argyrophilic, an attribute which makes this staining procedure particularly useful for the diagnosis of malignancy through study of the nuclear characteristics of the cell.

Riley *et al.*[25]: reporting upon a 3-year survey of the clinical and diagnostic use of this method, suggested that, compared with the normal polychrome methods, the silver impregnation technique may have the advantage of greater simplicity, rapidity, ease of examination, and the facility with which nuclear aberrations can be assessed. They conclude that these qualities, coupled with the observed accuracy resulting from an evaluation of smears taken from 2,008 cases, should be of value in the application of cytological methods to the detection of cancer.

Friedman[26] reported a new technique whereby the diagnosis of malignancy in cells obtained from the female genital tract may be made through the use of fluorescent dyes (fluorochromes). He claimed that cells stained with acidic and basic fluorochromes specifically stain certain cellular structures in a manner similar to the more generally used microscopic stains, such as haematoxylin and eosin and various other aniline dyes. Whereas cells stained with the latter dyes are usually examined by transmitted light, those stained by fluorochromes are practically colourless until irradiated by ultra-violet light. When subjected to this method of examination the cells fluoresce brightly and clearly with an enhanced definition of nuclear and cytoplasmic detail. The colour and degree of fluorescence are dependent on the characteristics of the stain of choice and the relative acidophilia and basophilia of the individual cells. Friedman described in some detail the application of this technique to the differentiation of normal from malignant cells by means of their morphological characteristics the degree of fluorescent brilliance, and the degree of variation of fluorescent colour in the nucleus and cytoplasm.

Runge *et al.*[27] and Zinser [28] suggested the use of phase-contrast microscopy as an alternative technique to that used by Papanicolaou in his cytological studies. Lash and Antonow,[29] using the phase-contrast microscope in the interpretation of fresh exfoliated material, claimed that this technique is in some cases superior in diagnostic accuracy to the Papanicolaou technique. Weid[30] also used phase-contrast microscopy as an office technique for the prescreening of vaginal smears and stated that, though this method serves the useful purpose of eliminating the high percentage of normal smears which would otherwise tax the cytologist's time, 'the fresh cell examination will not at the present stage of our knowledge be a substitute for the Papanicolaou technique in the cytologic laboratory'.

Shorr[31] describes a simple method of staining vaginal smears which we have found an excellent techinque for the assessment of oestrogen levels; the differential staining properties of this method are precise and cell counts of the cornified and uncornified elements can readily be made. While, however, the use of Shorr's stain is of the greatest value in the diagnosis of cyclic dysfunction through cell studies, it cannot be recommended for use where the presence or absence of malignant cells is to be determined.

The haematoxylin-and-eosin method of staining, as employed in routine histology, is commonly used, and in the early stages of our work on the detection of malignancy by means of exfoliative cytology we utilized this method to the exclusion of all others. In the determination of the grossly malignant smear its use was found to be adequate. Between the smear consisting entirely of normal cell-elements and that in which the cytological pattern was sufficiently defined to put the diagnosis of malignancy beyond doubt, were a very large number of smears presenting an indeterminate morphology, and in such cases the maximum clarity in the staining of nuclear and cytoplasmic detail was imperative if ambiguity in the classification of the atypical features was to be avoided. In these cases the limitation of the haematoxylin-and-eosin method of staining was very soon apparent and led to our abandoning this technique in favour of that advocated by Papanicolaou.[32]

Fixation of Smears. It is generally agreed that alcohol-ether fixation (equal parts of 95% alcohol and ether) affords the best results. Fixation is usually complete in 3-5 minutes, depending on the thickness of the smear, but as a routine procedure we have maintained a minimal period of fixation of 15 minutes and a maximum period of 3 days. Longer fixation does seem to affect the staining reaction of the cells as was suggested by Papanicolaou. Where ether is not available 95% alcohol may be used, although the results obtained with alcohol alone are not entirely satisfactory. Should it be necessary to post the slides to the laboratory for examination the method suggested by Ayre and Dakin[33] should be used. Smears are fixed in alcohol-ether for 15-30 minutes and then without being allowed to dry, covered with 2 or 3 drops of glycerine. A second cleaned slide is placed over the smear for protection and the two are then fastened by a rubber band, wrapped in greaseproof paper, and packed for posting.

Staining Technique. Consistent results in staining the smears is of paramount importance to the interpretation of the smear, and in this respect one procedure should be followed steadfastly until a standard staining method has been learned thoroughly. Only when this standard has been attained may the procedure be adjusted to meet the variations in the thickness of the smear. Macroscopic examination of the slide will readily indicate whether it should be left in the staining or other solutions for a shorter or longer period of time. The procedure we followed is, in all essential points, that advocated by Papanicolaou: the nuclear elements are stained with Harris' haematoxylin modified by the omission of glacial acetic acid, and the cytoplasm stained with two stains, viz. O.G.6 and either E.A.50 (which we prefer) or E.A.36. The principle components of E.A.50 and E.A.36 are light green yellowish, Bismarck brown, and eosin yellowish, in varying strengths contained in a 95% solution of alcohol. All staining solutions should be filtered, preferably immediately before use. When the stained smears begin to appear 'washed out' or to show change from the usual colour, fresh solutions must be prepared. It is essential to make mention here of 2 factors which will influence results to the extent, in some cases, of rendering the smear quite useless for examination:

(*a*) Every effort should be made to ensure that the most representative material is submitted for examination. The material obtained should be spread evenly on the slide.

(*b*) On no account should the smear be allowed to dry before fixation; the smear must be placed in the fixative *while still wet*. Failure to observe this point will modify the morphological characteristics to such an extent that it will be impossible to make accurate interpretation of the smear.

Cytological Diagnosis

Though it is unnecessary to present a detailed description of the normal cytology of the female genital tract, it is perhaps necessary to give a brief description of the more salient features in so far as they enter into diagnosis:

1. *Vaginal Cells.* Three main types of vaginal cells may be differentiated according to their place of origin in the vaginal epithelium. These are (*a*) superficial epithelial cells, (*b*) intermediate cells arising from the middle layer of the vaginal epithelium, (*c*) basal cells. In this last group may occasionally be seen features which make it difficult to distinguish them from abnormal cervical cells. Multinucleated cells may not infrequently be seen and mitotic forms are common. It is with the first group, i.e. the superficial vaginal cells, that we are more immediately concerned. These are large squamous cells with a small round or ovoid nucleus. In these cells may be seen changes in morphology, cytoplasmic staining reaction and nuclear form, which reflect the day-to-day variations in ovarian function during the normal menstrual cycle. This affords a simple method of following and evaluating the cycle of patients with disturbances of menstruation, anovulatory sterility, and other ovarian dysfunctions. Where these cells are entirely absent from the smear a marked impairment of ovarian function may be sought. Where oestrogenic function is marked or excessive, the squamous cell may be entirely cornified or keratinized. This is shown by their marked acidophilic staining reaction and nuclei that are pyknotic, shattered, or sometimes absent. When progesterone is being produced in addition to oestrogen, the cells often become folded, with their edges curled. This feature has occasionally been seen during a phase of oestrogen withdrawal. Further investigation is being carried on to assess the value of this aspect of exfoliative cytology. At this stage it is possible to state that where it is necessary to follow the response of the patient on oestrogen therapy, then exfoliative cytology is of very great value.

2. *Cervical Cells.* It is necessary here to stress the absolute importance of recognizing the fact that exfoliated cells from the cervix may have as their site of origin either the ectocervical or the endocervical region. The epithelium of the ectocervix is simply a continuation of the epithelium of the vagina covering that portion of the cervix up to the external os. From this junction, which demarcates the beginning of the endocervix, the pattern of the epithelium changes abruptly from the squamous to the columnar type of cell. It should be noted that it is in this area that carcinoma of the cervix most frequently originates; approximately 90% of cases are of the squamous-cell type, the remaining 10% owing origin to the glandular epithelium of the endocervix. It is often difficult, and sometimes impossible, to differentiate the cells arising from the ectocervix from those originating from the lower part of the vagina. There are, however, several factors by which the basal cells from the ectocervical region—the most important cells in the diagnosis of early carcinoma—may be recognized:

(*a*) These cells, which are ovoid or round, vary considerably in size and are generally basophilic in the staining reaction.

(*b*) Vacuoles, often quite large, are present, which tend to push the cytoplasm towards the periphery of the cell, thus giving the appearance of a heavy border. The nucleus, which also may appear ovoid or round, is frequently pushed to the periphery and is often dense, tending occasionally to exhibit an irregular or slightly flattened shape.

Perhaps the most characteristic distinguishing feature of the endocervical cell is the thin pale staining basophilic cytoplasm; the nucleus generally is round, centrally positioned, showing considerable variation in size, and very often containing a well-defined nucleolus.

3. *Endometrial Cells.* These are commonly found in the cervical and vaginal smear immediately before and after and during the menstrual period. In the intervening phase of the cycle they are rarely seen, except in the presence of a neoplasm or an inflammatory reaction or when endometrial hyperplasia is present. Endometrial cells are recognized as the smallest of the epithelial cells; they are generally round with a slight pale-staining cytoplasm. The nuclear outline is stained a heavy blue-black while the interior is pale staining and the chromatin granules dark staining and evenly distributed.

4. *Histiocytes.* These are rarely present in the normal vaginal smear. In inflammatory lesions, however, and benign and malignant neoplasms they are often found in very large numbers. The histiocyte constitutes one of the most difficult cells the cytologist has to contend with, since they are of many types and exhibit marked pleomorphism.

Cytological Criteria of Malignancy

Here it must be emphasized that there is no single feature in the examination of the smear by which a diagnosis of malignancy can be made. The interpretation of a positive smear must be made by the evaluation of various factors. There is no specific quality in any of the staining techniques in current use that enables a diagnosis to be made on the reaction obtained. The most valuable contribution to a positive diagnosis is provided by the nucleus; the changes in character are of greater significance than the alteration in the size and form of the cells or of the changes that are commonly found in the cytoplasm. The nuclear changes most frequently observed in the presence of malignant neoplasm may be enumerated as follows:

(*a*) Any variation in the nuclear size must carry significance.

(*b*) Abnormal nuclei frequently take a darker stain and thus appear more prominent. This is due to the darker staining of the chromatin granules, increase in the size of the granules, or changes in their distribution. Occasionally the chromatin collects around the nuclear border, giving an appearance of thickening to the nuclear membrane (Fig. 5).

(*c*) Variations in the shape of the nucleus are common and when present constitute a valuable diagnostic factor. The presence of bizarre shapes, giant nuclei and fragmented nuclei provide additional positive evidence.

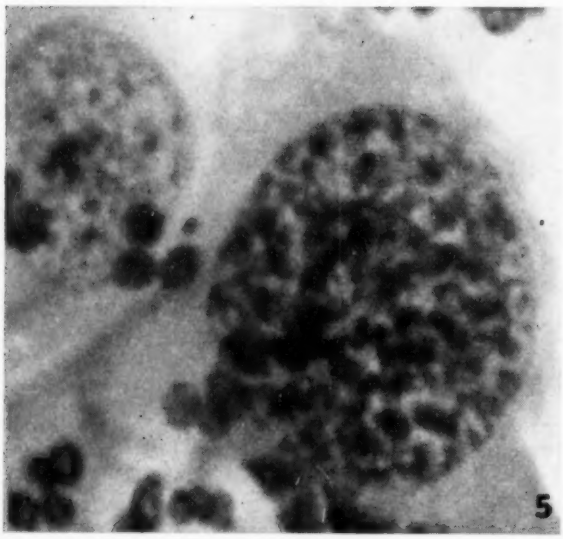

Fig. 5. Nuclei seen in smear reported upon as malignant, subsequently confirmed by histological examinations of surgical biopsy tissue as early squamous carcinoma of cervix. Note distribution and clumping of chromatin.

(*d*) Multinucleate cells demonstrating abnormal features are characterized by unequal and often distorted nuclei.

(*e*) Mitotic figures are of relatively little importance, since these may be found in the normal as well as in the abnormal smear.

Cytoplasmic Changes in malignancy are as follows:

(*a*) Abnormal cells are usually much larger than the normal cell, but though the cytoplasmic volume is increased, this increase is generally not proportionate to the increase in size of the nucleus.

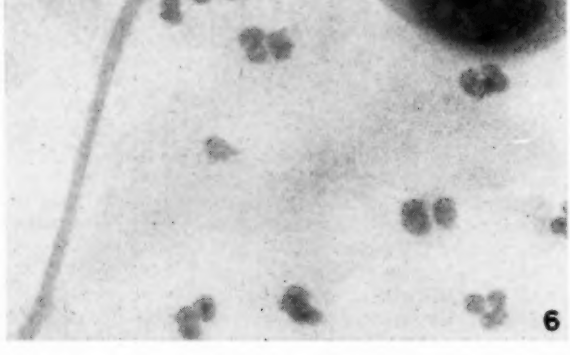

Fig. 6. 'Tadpole' cell from case of squamous carcinoma of cervix (case 1). Note distribution of chromatin with tendency to hyperchromatic staining.

(*b*) Gross abnormalities of shape with many bizarre forms are commonly seen, especially in squamous-cell carcinoma of the cervix. Despite the extreme individual variations there are certain general morphological patterns which tend to accompany specific types of malignancy. The 'tadpole' type of cell (Fig. 6) is frequently found in squamous-cell carcinoma; in poorly differentiated types embryonic forms may often be seen. In adenocarcinoma of the cervix the cells are generally of the round type, in spindle-cell carcinoma fibre-like cells are commonly found, whereas in endometrial cancer the cells are enlarged and the shape or form is usually more regular than in the cervical cells which, though commonly round, are often irregular in shape. Multinucleate giant-cell types are frequently seen in endometrial carcinoma (Fig. 7).

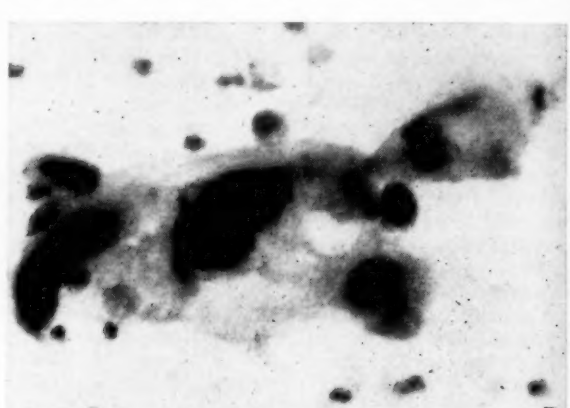

Fig. 7. Multinucleate giant-cell. Note hyperchromatic staining with thickening of nuclear border.

(*c*) Vacuolization: Large vacuoles, often irregular in shape and size, are frequently seen in malignant cells.

Clinical Procedure. For the past 18 months any patient found to have a cervical erosion is referred to a special clinic for further investigation (Louw[34]). Should the cervical lesions appear clinically malignant, the patient is then admitted to a ward for cervical biopsy, i.e. she is not primarily referred to the clinic. At the erosion clinic the cervix is inspected under a good light with the patient in the lithotomy position. Two smears are taken from each patient as previously described, viz. one by aspiration of the posterior fornix pool and one by Ayre's method.[18] After smears are taken, the cervix is cleaned, examined macroscopically and, in a large number of cases, studied with the aid of the colposcope, when particular attention is paid to the muco-cutaneous junction. Any irregularity of the mucosa is noted. After cleaning the vagina and cervix with N/10 acetic acid (Hinselmann), the mucosa is stained with Schiller's iodine solution and the areas which do not take up the

stain charted on the patient's clinic card. Wherever it appears necessary 'snips' are taken for histological examination. In the majority of cases the endocervix is cauterized with the 'hot-point' electric cautery and the eroded area is seared in a radial manner. Following cautery, an antiseptic cream is inserted. Antibiotic pessaries are prescribed for 10 nights to combat possible secondary infection. The patient is instructed to return in 6 weeks' time. At this visit the cervix is reviewed. Should cytological study reveal a positive or doubtful smear, arrangements are made for the patient's admission for diagnostic curettage and cervical cone biopsy.

Though the statistical analysis of the 1,050 cases constituting the basis of our survey is not complete, the following cases are reported as illustrative. The cases detailed here illustrate the type of case in which the study of exfoliated material has proved of value.

CASE REPORTS

Case 1

L.N., a 37-year-old married Bantu, attended at the Gynaecological Out-Patient Department on 1 March 1955 with a 3 months' history of a yellow irritating vaginal discharge, pain in the left iliac fossa, and dyspareunia. She had had 4 normal full-term deliveries, the last being 3½ years before her attendance at the clinic. Her periods were normal, with a regular 4/28 day cycle. No intermenstrual or post-coital bleeding had been noticed. Micturition was occasionally painful and for the last 3½ years she had suffered from stress incontinence. Her bowels were constipated. There were no relevant features in her previous history.

She was extremely obese and weighed 300 lb. No abnormalities were detected in the uterus or adnexa but speculum examination revealed a follicular-type erosion surrounding the external os.

The patient was referred to the erosion clinic, where smears were taken by the methods described. Cytological examination of the smears showed malignant cells to be present.

On receipt of this report arrangements were made for her admission to the ward. A biopsy was taken from the cervix and the uterus curetted. Histological examination revealed an early squamous carcinoma of the cervix.

Radiotherapy was administered, after which the cervix healed well, and the patient is now symptom-free. Subsequent smears show no evidence of malignancy.

Case 2

E.R., a 51-year-old married White woman, was first seen in the Gynaecological Out-Patients' Department on 18 January 1956 complaining of severe dysmenorrhoea and menorrhagia. On examination she was found to have a fibroid uterus the size of a 14 weeks' pregnancy and a chronic cervicitis with Nabothian follicles and a small erosion. Smears were taken from the cervix and, at the same time, the cervix was 'snipped'. The *Cytological report* (20 January) read 'marked atypicality of the cells, suggestive of malignancy'. The *histological report* of the biopsy specimen was 'carcinoma-in-situ'.

A total hysterectomy with the removal of a good cuff of vagina and right salpingo-oöphorectomy was performed on 6 February. Section of the cervix showed no evidence of malignancy.

Case 3

M.J., a 35-year-old married Coloured woman, attended on 8 March 1956 complaining of dysmenorrhoea and pain in the right side for 4 months and a watery white discharge for 2 months. On examination she was found to have a lacerated cervix with a large erosion; in addition she was thought to have an ovarian cyst. At the erosion clinic vaginal and cervical smears were taken and the cervix cauterized. Cytological examination of the smears (10 March) revealed the presence of malignant cells (Fig. 8).

The patient was admitted to the ward and on 25 May snips were taken from the anterior and posterior cervical lips. These were sent for histological examination and subsequently reported upon as '*chronic cervicitis only and no malignancy*'. More extensive

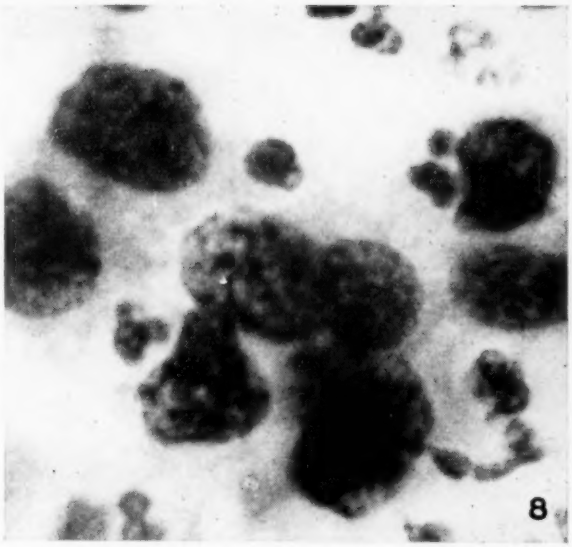

Fig. 8. Malignant cells from cervical smear on which diagnosis of carcinoma of cervix was based (case 3). Note hyperchromatic staining, thickening of nuclear membrane, and clamping of chromatin at nuclear border.

'snips' were taken 4 days later and in one of these, after multiple sections had been cut and examined, intra-epidermal carcinoma was reported (Fig. 9). The report added: 'Sections were cut at various levels and these show that the changes of intra-epidermal carcinoma are restricted to a small area in one of the two snips received'. In view of this finding it was decided to perform a total hysterectomy with removal of a vaginal cuff. At operation large bilateral simple ovarian cysts were found and total hysterectomy and bilateral salpingo-oöphorectomy was performed. Multiple sections from the cervix showed no evidence of malignancy.

Two further cases have been detected during September 1956. Mrs. B.M., aged 27 years and Mrs. M.M., aged 40 years, are

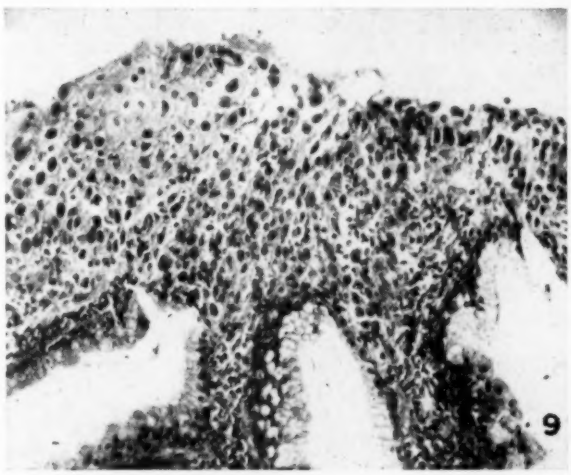

Fig. 9. Intra-epidermal carcinoma (case 3) revealed after multiple sections had been cut. The first surgical biopsy was reported as showing chronic cervicitis with no malignancy.

now undergoing further investigations. Both showed malignant cells on cervical smears and the histological report in both instances was carcinoma-in-situ.

DISCUSSION

Encouraging advances have been made over the last few years in the detection and treatment of early carcinoma of the cervix and uterus by the use of new diagnostic procedures made available by greatly improved laboratory techniques and a wider and deeper knowledge of cytology. Today the study of exfoliated material from the female genital tract is an established speciality in the practice of gynaecology. By this method of examination the cytologist is able to follow accurately normal and abnormal ovarian functions or detect the presence of malignant neoplasms, in many cases unsuspected. It is to the latter group of patients, i.e. those in whom no clinical manifestation of the disease is apparent, that cytology of exfoliated material will prove of greatest value and since 1941, when Papanicolaou and Traut[2] published the results of their investigations, there has been adequate confirmation of the value of this technique to justify its use as a screening method for the detection of carcinoma. Early reports of the method tended to over-simplification of technique and interpretation; it was, however, soon apparent that, with care and consistency in the method of taking the smear and (obtained through experience) in the method of staining and, more important, interpretation of the smear by a cytologist whose judgment had been developed through experience, an increasing number of highly accurate detection results could be obtained. The volume of figures published in recent years testifies to the value of the technique when its limitations are appreciated and interpretation of the smear is based on sound experience of cell morphology. The important question was not whether characteristic cells could be detected only in secretions from known and obvious cases of cancer, but whether they could be consistently detected in cases where no clinical evidence of carcinoma was present. The painstaking investigations by the earlier workers soon brought to light cases of unsuspected carcinoma.

Reicher, Massey and Bechtold,[35] who studied 3,500 vaginal smears and analysed the clinical and histological follow-ups of the patients, reported a combined error of 26 out of 3,500 cases, or 0·74%. These authors concluded that the study of vaginal smears is of value in the follow-up of carcinoma cases as well as in the detection of carcinoma in clinically benign cases.

Cuyler *et al.*[36] reporting on the cytological interpretation of 51,022 smears taken from 15,217 patients in a 4-year study, used Papanicolaou's technical procedures and classification, and considered that, provided the interpretations are properly controlled this method was of importance for screening purposes, its greatest value being the detection of early cervical carcinoma. They were of opinion that many intra-epithelial carcinomas of the cervix would be missed unless routine cystological studies were made on women as young as 20 years of age.

Pund and Aurbach,[37] who made microscopical examinations of serial sections of the external os of 1,200 surgically removed cervices, stated that they found pre-invasive carcinoma present in 47 of the cervices, an incidence of 3·9%. No pre-invasive carcinoma was seen on gross examination. The average age of the patients in whom pre-invasive cancer was found was 36·6 years, as compared to 48·6 years for definite invasive carcinoma cases, a *difference of* 12 *years*. Only 1 in 4 patients showed evidence of abnormal bleeding and in 80% of the sections examined there was microscopic evidence of normal-cycle endometrial function.

Though analysis of the cytological reports made on the 1,050 patients constituting our survey is not yet complete (it will form the basis of a further report in the near future) it may be stated that sufficient evidence has been obtained to prove the value of the cytology smear as an essential aid to the diagnosis of early malignancy. Detection of early carcinoma of the cervix is basically a microscopic technique; the difficulties experienced in the interpretation of the smear are similar to those faced by the haematologist in his examination of a blood smear. Diagnosis of the case is based, primarily, on the cytology of cells, whereas in histopathology the problem is somewhat simplified because not only is the cytology of the cells studied but also the orientation of these cells in the tissue. Taken as an adjunctive and complementary aid to the tissue biopsy, exfoliative cytology has a very definite place in gynaecology. Its value in the detection of the pre-invasive carcinoma will increase as a fuller understanding of cell morphology is gained. The salvage rate of surgery and radiation will thus be increased by a reduction of the delay in the application of the correct method of treatment. Theoretically all carcinoma cases would be curable if diagnosis were made early enough and proper treatment instituted immediately. Early detection is, therefore, the key to the control and cure of cancer.

Exfoliative cytology provides a technique the application of which causes no inconvenience or distress to the patient. The potentiality in large scale 'screening' of populations in cancer-prevention programmes, has not been fully explored owing in part, no doubt, to the shortage of adequately trained personnel. However, with the education of the public to the need, and value, of a check-up at regular intervals and the training of cytologists in sufficient numbers to interpret the smears, the technique may be expected to do much to reduce the terrible mortality from cancer. The study of the cell content of secretions from the female genitalia is an essential requirement in a progressive gynaecological unit for, as Papanicolaou[38] has stated, 'Should one attempt to evaluate the cytologic method and its general significance, he should bear in mind that it is still going through a period of evolution, and that our present achievements do not actually represent our maximum expectations in this new field. There is no doubt that the method possesses great potentialities, not only with regard to its practical usefulness in cancer diagnosis, but also in its more fundamental value as a new branch of the morphological sciences'.

CONCLUSIONS

1. The study of exfoliated cells, in secretions of the female genitalia, has a definite place in the practice of gynaecology.

2. It permits of the diagnosis of early cancer and, in some cases, of carcinoma-in-situ.

3. The various cyclic changes associated with normal and abnormal ovarian function may be accurately followed.

4. Bacteria, *Monilia* and *Trichomonas vaginalis* are clearly defined in smears stained by Papanicolaou's method.

5. It can be applied, as a screening method, on a large scale.

6. Detection of pre-invasive carcinoma coupled with immediate treatment must, inevitably, reduce the mortality figures associated with this disease.

7. The simplicity of the technique, its reliability in experienced hands, with the lack of inconvenience and distress to the patient in its application, ensures the use of the method in every progressive gynaecological unit.

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HAEMOLYTIC ANAEMIA IN DISSEMINATED LUPUS ERYTHEMATOSUS

REPORT OF A CASE

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Anaemia is commonly associated with disseminated lupus erythematosus. Michael *et al.*[1] studied case records of 86 patients with lupus erythematosus, and investigated 25 cases of their own. Of the 111 patients, 87 were anaemic. Although the pathogenesis of the anaemia accompanying this disease is obscure in most cases, in some it is definitely due to abnormal haemolysis of the red blood-cells. Dacie[2] considers it likely that minor degrees of haemolysis would frequently be found if careful erythrocyte survival studies were carried out.

The patient may present clinically as a haemolytic anaemia, with or without other manifestations of lupus erythematosus. The haemolytic anaemia is usually of the auto-immune type, in that the erythrocytes show evidence of sensitization, and anti-erythrocyte antibodies are often demonstrable in the serum. Wiener[3] demonstrated the presence of auto-antibodies in the serum of such a patient by using trypsinized erythrocytes. Zoutendyk and Gear[4] mentioned that the direct anti-globulin test was positive in 4 out of 5 patients investigated by them. Michael *et al*[1] found that 25% of their cases showed erythrocyte sensitization, and 3 out of 25 had overt haemolytic anaemia. Pisciotta *et al.*[5] found 1 out of 7 cases complicated by haemolytic

anaemia associated with a positive direct antiglobulin test. These authors also showed that the anti-erythrocyte antibodies and the L.E. factor in the serum were not the same. Evans *et al.*[6] mentioned 4 cases of lupus erythematosus, all associated with positive direct antiglobulin tests. All 4 cases described by Baikie[7] had positive direct antiglobulin tests, and one was complicated by haemolytic anaemia. In this case warm auto-agglutinins were present in the serum. Dacie[2] carried out direct antiglobulin tests on 9 patients with lupus erythematosus. The reaction was strongly positive in 1 patient suffering from overt haemolytic anaemia, and weakly positive in 5 out of the remaining 8 patients. In each instance the reaction appeared to be of the 'cold' antibody type.

CASE REPORT

The patient, a European female aged 46, was admitted to hospital for investigation. She complained of a rash on her hands and forearms, which had started 11 months previously. On the day preceding the onset of the rash she had washed clothes in washing-soda, which she considered to be the cause of the rash. The skin lesion became progressively worse, but she did not seek medical advice until 9 months after it had started, when she began to feel generally off-colour, with anorexia and bouts of nausea. She had also developed a persistent cough. These systemic symptoms became progressively worse, and 2 months later she was admitted to hospital.

Physical Examination

The patient was obviously ill. Her skin had a sallow colour, and her temperature was 100·4°F. The conjunctivae were pale and jaundiced. A scaly erythematous rash was present on both hands and forearms, mainly on the dorsal aspects. There were irregular areas of brown pigmentation over the front of the chest and forehead. Examination of the respiratory system revealed a left-sided basal lobar pneumonia; rhonchi and fine crepitations were also audible in the upper lobe on the left side. Her blood pressure was 110/55 mm. Hg, and a soft systolic murmer could be heard over the whole praecordium. The spleen and liver were not palpable. No other significant abnormality was detected on clinical examination.

Laboratory Investigations

1. *Haematological.* On admission there were 1,310,000 erythrocytes per c.mm., with 3·6 g. of haemoglobin per 100 ml. The PCV was 12·0%, and the MCHC 30%. There were 28,200 leucocytes per c.mm., with 68% neutrophils, 0·5% monocytes, 11·5% lymphocytes, 0·5% neutrophil metamyelocytes, 2·0% staff cells, 0·5 plasma cells, and 17% late normoblasts. The neutrophil leucocytes showed a shift to the left. The reticulocyte count was 24·4%. Examination of a blood film showed severe diffuse basophilia, anisochromia, anisocytosis and poikilocytosis.

2. *Biochemical.* The urine contained urobilin (4 plus); bilirubin and urobilinogen were absent. Microscopic examination showed no abnormality. The serum-bilirubin concentration was less than 0·5 mg. per 100 ml., and the total serum proteins 8·5 g. per 100 ml., with 3·7 g. albumin, 4·8 g. globulin and 1·82 g. gamma globulin. Liver function tests gave the following results: Thymol turbidity 6·0 units, thymol flocculation 4 plus, zinc-sulphate turbidity 30·0 units.

3. *Serological.* The following serological investigations were done, all with negative results (these are carried out by us on all cases of 'idiopathic' haemolytic anaemia): Agglutination reactions for typhoid and paratyphoid, rickettsial complement-fixation tests, virus complement-fixation tests, kolmer cardiolipin test for syphilis. Three weeks after admission to hospital L.E. cells were found in large numbers on specially prepared blood-smears, establishing the diagnosis as lupus erythematosus.

4. *Immuno-haematological.* The patient was group A Rh positive (CcDE). The direct antiglobulin test was strongly positive. The quantitative antiglobulin test (Dacie[2]) gave a reaction of the 'warm' antibody type (Table I). Abnormal antibodies were demonstrated in the patient's serum, with the indirect antiglobulin technique as well as with trypsinized and 'ficinated' cells. Although active at 37°C, the antibodies showed a marked increase in activity with a reduction in temperature (Table III). After inactivation of the serum by heating at 56°C for 30 minutes (to destroy the complement) the indirect antiglobulin test was negative on cells sensitized at 4°C for 1 hour, but still positive when sensitized at 37°C (Table IV). The inability of antibodies to sensitize red blood-cells in the absence of complement is considered to be characteristic of the 'cold' type. Incomplete cold antibodies were present to a titre of 64 with the indirect antiglobulin technique, after sensitization of the cells at 4°C (Table II). Agglutination of the enzyme-treated cells occurred despite the absence of com-

TABLE I. THE QUANTITATIVE ANTIGLOBULIN REACTION

Dilutions of antiglobulin serum				
1 *in* 4	1 *in* 16	1 *in* 64	1 *in* 256	*Control (saline)*
+	+	++	+++	negative

+ denotes weak agglutination; +++ denotes strong agglutination

TABLE II. TITRATION OF THE INCOMPLETE COLD ANTIBODY WITH THE INDIRECT ANTIGLOBULIN TECHNIQUE (SENSITIZATION AT 4°C)

Dilutions of the patient's serum						
1 *in* 1	1 *in* 2	1 *in* 4	1 *in* 8	1 *in* 16	1 *in* 32	1 *in* 64
++++	++++	++++	+++	+++	++	+

++++ denotes strong agglutination; + denotes weak but definite agglutination

TABLE III. TITRATION OF THE ANTIBODIES AGAINST ENZYME-TREATED ERYTHROCYTES AT VARIOUS TEMPERATURES (SENSITIZATION FOR 1 HOUR)

		Dilutions of the patient's serum					
		1 *in* 1	1 *in* 2	1 *in* 4	1 *in* 8	1 *in* 16	1 *in* 32
4°C	Ficinated	+++	++	++	+	+	−
	Trypsinized	++	++	+	+	(+)	−
20°C	Ficinated	+	+	(+)	−	−	−
	Trypsinized	+	(+)	−	−	−	−
37°C	Ficinated	+	(+)	−	−	−	−
	Trypsinized	(+)	−	−	−	−	−

+++ denotes strong macroscopic agglutination; (+) denotes weak microscopic agglutination.

TABLE IV. THE INDIRECT ANTIGLOBULIN REACTION CARRIED OUT WITH ACIDIFIED AND INACTIVATED SERUM

	Temperature of erythrocyte sensitization		
	4°C	20°C	37°C
Unacidified normal serum	++++	+	+
Acidified serum ..	++++	++	+
Inactivated serum ..	—	—	+

++++ denotes strong agglutination; + denotes weak agglutination.

plement (Table V). Haemolysins could not be demonstrated at 37°C or at room temperature, even after acidification of the patient's serum. As is often the case in auto-immune haemolytic anaemia, group specificity of the antibodies could not be demonstrated; erythrocytes of a selected panel of donors were all agglutinated. Ham's acid-serum and the indirect Donath-Landsteiner tests were negative.

Treatment and Progress

During the initial period of hospitalisation, before the diagnosis had been established, the patient was treated with numerous antibiotics. Apart from some amelioration of the respiratory condition little improvement resulted. Treatment with Meticorten (prednisone) was started after 12 days because of the inadequate response to antibiotics. The patient also received a transfusion of 1,500 c.c. of whole blood, without any apparent reaction. The dermatitis responded dramatically to this therapy and after 10 days there was no evidence of abnormal haemolysis. This coincided with the disappearance of the warm auto-antibody, although the incomplete cold antibody was still present, and the direct antiglobulin test still positive.

The patient was discharged about 2 months after admission, with 11·6 g. of haemoglobin per 100 ml. and no evidence of abnormal haemolysis. The direct antiglobulin test was still positive. The persistence of a positive direct antiglobulin reaction is frequently found in treated and clinically cured cases of auto-immune haemolytic anaemia.

DISCUSSION

In lupus erythematosus the appearance of the skin lesion after exposure to an irritant is not uncommon. King-Smith[8] reported 18 cases in which dermatitis followed external irritation. Development of the skin lesion after exposure to sunlight has also been described.

The immuno-haematological picture was interesting in that the antibody which was active at 37°C was not affected by inactivation of the complement (Table IV), suggesting the presence of two separate antibodies, and not an incomplete cold antibody with a high thermal amplitude. It was this 'warm' antibody which was sensitizing the patient's cells, as evidenced by the 'warm' type of reaction with the quantitative antiglobulin test. The incomplete cold antibody appeared to play no part in the causation of the abnormal haemolysis.

It is interesting to note that inactivation of the complement has little, if any, effect on the ability of the incomplete cold antibody to agglutinate enzyme-treated erythrocytes, and yet completely inhibits its ability to sensitize a saline suspension of erythrocytes to antiglobulin. This indicates that the antibody is thermostabile (as is the case with incomplete warm antibodies) and that only the complement is destroyed by heating at 56°C for 30 minutes. Why complement should be necessary in the one instance and not the other is uncertain.

The haemolytic process in lupus erythematosus responds well to steroid therapy. Michael *et al.*[1] reported good response to such therapy, although the haematological improvement was not quite so dramatic as the clinical improvement. Baikie *et al.*[7] reported amelioration of the haemolytic process, with disappearance of the auto-agglutinin. Pisciotta *et al.*[5] also found that cortisone therapy resulted in improvement of the symptoms, and a gradual decline in the rate of blood destruction.

In this patient treatment with Meticorten resulted in fairly rapid cessation of the haemolytic process, with disappearance of the 'warm' antibody from the plasma. The skin lesion and constitutional symptoms also improved dramatically.

Comment

The aetiology and pathogenesis of lupus erythematosus has not been elucidated. That it has an auto-immunologic basis is suggested by: (1) The abnormal facility with which patients produce antibodies. (2) Abnormal response to drugs and sunlight. (3) The frequency with which false positive serological reactions occur. (4) The occurrence of hyperglobulinaemia. (5) The high incidence of cases which show erythrocyte sensitization with multiple antibody production. The relative frequency with which auto-immune haemolytic anaemia complicates the disease is in keeping with this concept.

TABLE V. TITRATION OF THE ANTIBODY ACTIVITY AGAINST TRYPSINIZED AND FICINATED CELLS, BEFORE AND AFTER INACTIVATION OF THE COMPLEMENT

			Dilutions of the patient's serum					
			1/1	1/2	1/4	1/8	1/16	1/32
Before Inactivation	4°C	Ficinated	+++	++	++	+	+	—
		Trypsinized	++	++	+	—	—	—
	20°C	Ficinated	+	+	(+)	—	—	—
		Trypsinized	+	(+)	—	—	—	—
After Inactivation	4°C	Ficinated	++	++	+	+	(+)	—
		Trypsinized	+	+	(+)	—	—	—
	W 20°C	Ficinated	+	+	(+)	—	—	—
		Trypsinized	+	(±)	—	—	—	—

+++ denotes strong agglutination, + weak macroscopic agglutination, and (+) agglutination which is only visible microscopically.

As the disease process may precede its clinical manifestations by several years, it must be excluded in every case of 'idiopathic' auto-immune haemolytic anaemia.

Since the haemolytic process usually responds well to steroid therapy, it should always be given a full clinical trial before splenectomy is considered.

SUMMARY

A case of auto-immune haemolytic anaemia complicating lupus erythematosus is presented. The immuno-haematological findings and the treatment are discussed.

I am grateful to Dr. A. Zoutendyk for his helpful criticism.

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PROVINCIAL ADMINISTRATION OF THE CAPE OF GOOD HOPE

INTRODUCTION OF CHARGES FOR HOSPITAL SERVICES

The following circular was issued to all Medical Superintendents of Provincial Hospitals, Chairmen of Hospital Boards and others on 15 November 1956, and a finalizing circular indicating amendments in the circular (which are embodied in the following copy of the circular) was issued on 8 December.

1. I attach a copy of the Hospitals Further Amendment Ordinance No. 22 of 1956, and have to invite your attention to Section 5* thereof.

Authority for the raising of charges for Hospital Services

2. It will be observed that this section substitutes a new section for section 40 of the principal ordinance and empowers the Administrator to raise charges for hospital services.

Date of Coming into Operation

3. With the exception of Section 7 of the amending ordinance which deals with the Hospital Development Fund and which came into operation on 1 April 1956, the ordinance will come into operation on 1 January 1957, and charges for hospital services are to be raised as from that date.

Tariff of charges for hospital services to in-patients

4. The charges for hospital services (as defined in Section 3 of the attached amending ordinance) to in-patients accommodated in private and semi-private wards are to be as follows:

Private Ward (1 bed) .. 30/– per day.
Semi-private (2 beds) .. 25/– per day.

5. The charges for hospital services, as defined, to in-patients who are accommodated in general wards are based upon the incomes of the patients and, in the case of a single person who has no dependants, are as follows:

Income (to nearest completed £)	*Charge*
Below £20 per month	One cash payment of 10/– upon admission and no further charge. (Hereafter referred to as the Nominal Charge).
From £20 to £29 per month ..	5/– per day.
From £30 to £39 per month ..	10/– per day.
From £40 to £49 per month ..	15/– per day.
£50 per month and over ..	20/– per day.

Allowances for married persons and those having dependants

6. Where a patient has a dependant or is married, his income is to be reduced for the purposes of assessment by £10 per month for each dependant, for which purpose a wife (or husband in the case of a female patient) is to be regarded as a dependant.

Tabulated general ward tariff

7. Tabulated, the general ward tariff is as follows:

Income	*Single*	*Married with no children or single + 1 dependant*	*Married + 1 child or single + 2 dependants*	*Married + 2 children or single + 3 dependants*
Below £20 per month	Nominal charge i.e. one cash payment of 10/–	Nominal charge i.e. one cash payment of 10/–	Nominal charge i.e. one cash payment of 10/–	Nominal charge i.e. one cash payment of 10/–
Per month				
£20–£29	5/– p.d.	"	"	"
£30–£39	10/– p.d.	5/– p.d.	"	"
£40–£49	15/– p.d.	10/– p.d.	5/– p.d.	"
£50–£59	20/– p.d.	15/– p.d.	10/– p.d.	5/– p.d.
£60–£69	20/– p.d.	20/– p.d.	15/– p.d.	10/– p.d.
£70–£79	20/– p.d.	20/– p.d.	20/– p.d.	15/– p.d.
£80–£89	20/– p.d.	20/– p.d.	20/– p.d.	20/– p.d.

Space does not permit of further tabulation but the above is sufficient to indicate the basis of assessment. The table should obviously be extended according to the number of dependants, e.g. a married man with three children.

Definition of Income

8. For the purposes of paragraphs 5, 6 and 7 above, fractions of a £ in a patient's income are to be disregarded.

9. For the purpose of assessment, the patient's statement of his income is to be accepted at the time of admission.

10. In the case of married persons, income is to be regarded as the income of the husband and wife.

11. In the case of dependent minor patients, income is to be regarded as the income of the patients' parents.

12. In the case of parents who live with adult sons or daughters, income is to be taken as the income of the parents only.

13. (*a*) In the case of persons who are paid on a weekly basis, their monthly income for purposes of assessment should be deemed to be four times their weekly pay.

(*b*) Where a patient's income is received annually, his monthly income for purposes of assessment should be deemed to be one twelfth of his annual income.

Relief to long term general ward patients

14. The charge payable by a patient who is accommodated in

* See page 1214 of this issue of the *Journal*.

a *general* ward, excluding the categories referred to in paragraphs 26-30, is to be reduced as follows:

By 25% for any period over and above 30 days *continuous* stay in hospital.

By 50% for any period over and above 60 days *continuous* stay in hospital.

The granting of this relief may, however, be withheld by a hospital board if, on good and sufficient grounds, it deems the granting of relief to be unnecessary in any particular instance.

Patients accommodated in private wards on medical grounds etc.

15. Where a patient is accommodated in a private or semi-private ward because his condition necessitates it or because accommodation in a general ward is not available, he is to be held liable only for the charges he would have had to pay had he been accommodated in a general ward.

Reduction and waiving of charges by boards

16. The Administrator has delegated power to all hospital boards in terms of Section 40 (4) of the Ordinance, as amended, to reduce or waive, upon application by individual general ward in-patients, the charges levied against them for hospital services.

17. Hospital boards will not be permitted to reduce or waive the charges payable by or in respect of patients who

(*a*) are accommodated in private or semi-private wards, except in the case of the patients referred to in paragraph 15 above;

(*b*) fall within the provisions of the Workmen's Compensation Act, 1941, or the Motor Vehicle Insurance Act, 1942;

(*c*) are infectious cases accommodated on behalf of a local authority; or

(*d*) are accommodated in terms of any special agreement which may have been entered into by the Administration.

Assessment of charges and procedure for the reduction or waiving thereof

18. All in-patients are to be assessed upon admission on their own incomes or, in the case of dependent minors, those of their parents or guardians irrespective of who is to meet the charges, in accordance with the tariff of charges set out above.

19. Where a general ward in-patient cannot pay the charges assessed against him, he may appeal to the hospital board to have the charges reduced or waived and the board's decision in the matter will be final. Applications for relief are to be made upon a form prescribed for the purpose, for the printing of which this office is arranging.

Legal action for the recovery of charges and writing off of charges

20. The responsibility for taking legal action for the recovery of charges and for writing off irrecoverable charges in cases where the boards have not waived the charges is to remain that of the Administration at this stage.

Special classes of in-patient

21. (*a*) Short-term cases accommodated in *general* wards who are in hospital as at 31 December 1956 should continue to receive hospital services free of charge for the duration of their stay in hospital provided that this does not extend beyond 31 January 1957. Should there be any such cases still in hospital after this date, they should be assessed and required to pay for hospital services as from 1 February 1957.

(*b*) Patients accommodated in private and semi-private wards who are in hospital as at midnight on 31 December 1956, should be required to pay the charges prescribed in paragraph 4 above as from 1 January 1957.

22. Patients for whom the Government, a local authority or other body is responsible, such as inmates of trade schools, reformatories, gaols, members of the S.A. Police, Union Defence Force, Sick or Medical Aid Funds etc., are to be assessed on their incomes notwithstanding the fact that the Government, local authority etc., may be responsible for meeting the charges. This policy is to be applied also to orphans who are inmates of orphanages but not to those who live with guardians in whose cases the incomes of the guardians are to be taken as the deciding factor.

23. Cases such as foreign sailors, airmen, etc. in transit, are to be assessed on their own incomes but the accounts for their hospitalisation should be submitted for settlement to the companies by which they are employed.

24. (*In regard to the Education Department's scheme for the medical treatment of necessitous pupils.*)

25. Patients who are detained in or required to re-visit *medical teaching hospitals* because their presence is required *for teaching purposes* are not to be charged in respect of the period they are detained in hospital after the date upon which they would normally have been discharged nor in respect of such subsequent visit or visits as they may be requested to make.

26. Cases falling within the provisions of the Workmen's Compensation Act, 1941, are to be charged at the rates agreed to from time to time by the Commissioner. At present these are—

Europeans, Coloureds, Asiatics .. £2 0s. 0d. per day
Natives .. .. £1 15s. 0d. per day

27. In respect of employees of the Administration who are injured on duty, the charges applicable to cases falling under the Workmen's Compensation Act, 1941, should be raised but the accounts should be referred for settlement to the appropriate department of the Administration.

28. Cases falling within the provisions of the Motor Vehicle Act, 1942 are to be charged at a rate based on the actual daily cost. Until further notice this charge is to be £2 0s. 0d. per day.

29. Where standard agreements for the conduct of infectious diseases blocks have been entered into with local authorities, the charges for infectious cases should be in terms of the agreements.

30. Where no standard agreements exist, the charge for all other infectious cases should be at a rate based on the actual daily cost. Until further notice the charges to be raised should be £2 0s. 0d. per day.

31. All nurses in the employment of provincial hospitals (excluding those engaged from nursing agencies), members of the honorary medical staff and all persons falling within the provisions of the Hospital Board Service Ordinance No. 19 of 1941, are to be given hospital services free of charge at all provincial hospitals. This concession does not extend to the members of their families.

New admission form

32. A new admission form is being drafted, supplies of which will shortly be issued. It will not be necessary for patients requesting private or semi-private ward accommodation or patients paying in full to complete the portion of the admission form dealing with income.

Patients unable to pay

33. Where a person liable for payment of the Nominal Charge of 10/- is found at the time of admission to be totally indigent and unable to make even this payment, he should nevertheless be admitted and should on no account be refused admission because he is unable to pay.

Medical Treatment

34. It will be observed from sub-section (6) of the new section 40 of the Ordinance (see section 5 of the attached Hospitals Further Amendment Ordinance) that a patient who is liable for payment of the Nominal Charge i.e. for payment of less than five shillings *per day* for hospital services may not select his own medical practitioner, but must accept the services of the hospital's medical staff. There are two exceptions to this general rule, namely—

(*a*) Where some person or body other than the patient engages the medical practitioner, such medical practitioner should be permitted to attend the patient. Examples of this type of patient are the Sick Fund/Medical Aid case, the employee whose employer has a standing arrangement with a medical practitioner to attend his employees etc.

(*b*) Where a patient is liable for payment of the Nominal Charge i.e. for payment of a charge of less than five shillings *per day* on assessment based on his income but wishes to have his own medical practitioner, he may have such practitioner provided that he pays five shillings *per day* for hospital services notwithstanding the assessment of his liability.

35. Patients paying five shillings or more *per day* for hospital services should engage their own medical practitioners except at hospitals which have been 'closed' in terms of Section 40 (7) of the Ordinance.

36. The certificate of inability to pay for medical treatment at present in use falls away as from the introduction of charges for hospital services since patients paying the Nominal Charge i.e. less than five shillings *per day* will normally be treated by the medical staff of the hospital and the settlement of the accounts for the medical treatment of those paying five shillings per day and over is entirely a matter between the patients and their medical practitioners.

Charges for Hospital Services to out-patients

37. A charge of 1s. 0d. per visit is to be raised for hospital services rendered to out-patients at all out-patient departments attached to provincial hospitals and at detached dispensaries and clinics where patients are attended to by medical practitioners.

38. The charge for out-patient services is to be paid by all out-patients i.e. by both Europeans and non-Europeans.

Board to meet out-patient charge where patients are unable to do so

39. Where an out-patient is totally indigent and unable to meet the charge for out-patient services, his treatment is to be sponsored by the hospital board and the charge met by the board from the percentage of the fees it receives in terms of Section 40 (8) of the Ordinance, as amended.

Note: (*a*) Since this expenditure by the boards will be subsidisable in terms of Section 46 of the Ordinance (Section 8 of the amending ordinance* attached), the boards will in effect be required to sponsor out-patient services to the totally indigent to the extent of only sixpence per visit.

(*b*) Whilst the charge for out-patient services has been fixed at a figure which should be well within the means of the patients, it is realised that in certain areas and under certain exceptional circumstances this may not prove to be the case. Should such exceptional circumstances arise, the board should inform me of the fact.

Boards not empowered to reduce or waive out-patient charges

40. Hospital boards are not empowered to reduce or waive the charges raised against out-patients.

District Nursing and Midwifery Services

41. With the exception of the type of case referred to in paragraph 42 below, no charge should be raised for the services rendered by district nurses or midwives, whether these are rendered at the homes of the patients or in the district rooms of the nurses.

42. As you are aware, it is the function of district nurses and midwives to undertake domiciliary and district room nursing under the overall supervision of the medical superintendents. It is not their function to nurse the private patients of private doctors and they should not normally be permitted to do so. Such patients should employ private nurses or make other arrangements. It is realised, however, that exceptional circumstances may arise where private nurses cannot be obtained and in such cases medical superintendents may in their discretion permit the use of the services of the district nurse or midwife provided that the patient pays for her services at the rate of 10s. 0d. per visit and, in addition, pays for her transport at the rate of 8d. per mile in respect of the mileage travelled by her outside a radius of five miles from her headquarters for the purpose of each visit.

Percentage of fees to be paid to boards

43. In terms of Section 40 (8) of the Ordinance, as amended, hospital boards are to receive 7½% of the total payments made to the Administration for hospital services excluding payments made in respect of—

(*a*) patients falling within the provisions of the Workmen's Compensation Act, 1941, or the Motor Vehicle Insurance Act, 1942;

(*b*) infectious cases accommodated on behalf of local authorities;

(*c*) patients accommodated in terms of any special agreement which may have been entered into by the Administration; and

(*d*) patients generally whose outstanding accounts have been handed over to this office for collection.

44. Payment to hospital boards of the percentage referred to in the preceding paragraph is to be effected by the medical superintendents monthly.

Period of validity

45. The contents of this circular will apply as from the 1st January, 1957, and will be subject to review at any time.

Conflict with previous circulars

*See page 1214 of this issue of the *Journal*.

46. In the event of conflict ,the provisions of this circular will take precedence over those of previous circulars as from the 1st January, 1957.

Miscellaneous

47. This circular has been confined to matters of policy and a further circular will shortly be addressed to all medical superintendents dealing with the practical implementation of the decision to raise charges, procedure to be followed, etc. Until such time as they have received and studied it, medical superintendents are asked not to inundate this office with procedural enquiries as the probability is that their queries will be fully dealt with in the circular referred to.

48. A further circular is also being issued regarding the subsidisation of hospital board funds.

HOSPITALS FURTHER AMENDMENT ORDINANCE NO. 22 OF 1956

Section 5. The following section is hereby substituted for section *forty* of the principal ordinance:

40. (1) The Administrator may prescribe tariffs of charges to be paid for hospital services and the conditions on which and circumstances under which a patient in a provincial hospital shall receive free treatment.

(2) In framing tariffs of charges for hospital services, the Administrator may vary such charges according to the particular class or classes of patients receiving hospital services or the nature of the accommodation and facilities supplied, or other circumstances, and may prescribe that under certain circumstances no charge shall be payable.

(3) The Administrator may reduce or waive the charge for hospital services payable in respect of any person if he is satisfied that such person, or any other person responsible or legally liable for such person's charges, is not able to pay in full the charges prescribed or any charges at all, as the case may be.

(4) The Administrator may authorize, subject to such conditions as he may prescribe, Boards in general or any particular Board to exercise the powers conferred on him by sub-section (3) hereof.

(5) A patient in a provincial hospital may select and engage his own medical or dental practitioner, provided that—

(*a*) the Administrator shall not be liable for the payment of any fees due to such practitioner,

(*b*) such practitioner is not a whole-time member of the staff of any provincial hospital.

(6) Notwithstanding the provisions of sub-section (5), a patient, other than such patient on behalf of whom some other person or body pays the medical or dental practitioner, who is liable to pay a charge for hospital services of less than five shillings per day shall not select and engage his own practitioner.

(7) Notwithstanding the provisions of sub-section (5), a patient in any provincial hospital or portion thereof which the Administrator may designate, shall not select and engage his own practitioner.

(8) The Administrator shall pay to a Board an amount equal to seven and a half *per centum* of the total payments made to the Administration for hospital services rendered at a provincial hospital in respect of which such Board has been appointed, provided that payments made on behalf of a patient in respect of whom compensation is paid under the Workmen's Compensation Act, 1941, and such other payments as the Administrator may determine, shall be excluded from such total payments."

Section 8. The following section is hereby substituted for section *forty-six* of the principal ordinance:—

46. The Administration may pay to a board a subsidy of an amount not exceeding fifty *per centum* in respect of expenditure incurred on purposes approved by the Administration.

PASSING EVENTS : IN DIE VERBYGAAN

Karroo Division, Cape Western Branch. A meeting of this Division was held at the Masonic Hotel, Beaufort West, on Saturday, 1 December, when a team of speakers from Cape Town, consisting of Prof. E. C. Crichton, Mr. J. A. Currie and Mr. Hamilton Bell visited the town. Mr. P. J. M. Retief, who organized the programme, also attended. The Chair was taken by Dr. P. J. Fischer of Beaufort West, President of the Division. Professor Crichton spoke on Postmaturity, Mr. Currie discussed Closed Injuries of the Urethra and Mr. Bell spoke on a variety of conditions affecting the Hip Joint. After the addresses an active

discussion by members of the Division took place. The meeting was followed by a social dinner and the occasion was much enjoyed by members and visitors. Much enthusiasm and activity is still shown in this newly established Division.

* * *

Dr. W. James Latham, O.B.E., F.F.R., of 85 St. George's Street, Cape Town, has been appointed by the Admiralty to be 'Consultant in Radiology to the Royal Navy in South Africa'.

* * *

Dr. Benjamin Chesler. Dr. Alice Cox having retired from private practice, Dr. Chesler will be joining Drs. Max Feldman, Carl Jeppe and Fred Frankel in psychiatric practice at 1 Keyes Court, Keyes Avenue, Rosebank, Johannesburg, in December 1956. Branch consulting rooms will be maintained at Dr. Chesler's previous address, Dunvegan Chambers, Joubert Street, Johannesburg. Telephone numbers: 1, Keyes Court, Rosebank, 42-2481, 42-2154; Dunvegan Chambers, 23-7490.

* * *

Dr. and Mrs. C. Merskey have left for the United States via Rome and will be away for 7 months. Dr. Merskey who has been awarded a Rockefeller Travelling Scholarship and whose main interest is in haematology hopes to visit clinics both in the Middle West and on the Pacific Coast.

REVIEWS OF BOOKS : BOEKRESENSIES

HISTOLOGY

Histologie und Mikroskopische Anatomie des Menschen. Zweite verbesserte Auflage. By Wolfgang Bargmann. Pp. xv + 796. 640 Illustrations. DM 69.60. Stuttgart: Georg Thieme Verlag. 1956.

Contents: Zellen- und Gewebelehre. A. Die lebendige Masse. B. Die Gewebe. Organe und Systeme. A. Der Bewegungsapparat. B. Das Kreislauf- und Abwehrsystem. C. Das innersekretorische System. D. Der Verdauungsapparat. E. Die Atmungsorgane. F. Die Harnorgane. G. Die Geschlechtsorgane. H. Die Haut. J. Die Sinnesorgane. K. Das Zentralnervensystem.

This large volume is a fine work from every point of view. The German medical student who uses it must have a very comprehensive grasp of the histology of the human body. The earlier chapters deal with the structure of the various type of cells, their growth, multiplication and death. Thus, in turn we read of the finer structure of the various types of epithelial cells, of elastic tissue, bone cells, fixed tissue cells—all in great detail and splendidly illustrated. Further chapters take each system in turn; the muscular system, nervous system, glandular, excretory, reproductory, etc.

Most of the illustrations are in black-and-white and many are schematic, showing clearly in 3-dimensional form the composing elements of the organ discussed. For example, the drawing of the ductus deferens shows the very complicated system of intertwining and spiraling bundles of muscle fibres which provide for the special function of this canal. The representation of the Haversian system in bones is a model of clarity which makes the reading of the text an easy matter. Some of the magnifications are of low order, the tissue or cell arrangement under discussion being presented as seen with a hand lens, so that the student's sense of proportion is not distorted too much by the photomicrographs taken with the electronic microscope, of which a few are reproduced. These latter obtain a magnification of several thousands. The reviewer, as a student, was content with a simple concept of cilia. But the student of this book is given longitudinal sections of these minute processes to study; they show a fairly complicated structure in themselves. No doubt further magnifications of what, in a picture magnified 90,000 times, appear as tiny dark corpuscles, would reveal still further wonders.

The object of the book, however, is not to tempt the reader into fanciful speculation, but to lay a sound foundation of the structure of the human body in conformity with present-day needs and knowledge; this it does admirably. Indeed, it is no exaggeration to say that a careful study of the illustrations and the captions accompanying them would in itself build up a useful store of knowledge.

The section of the central nervous system unfortunately does not contain any of those 3-dimensional schematic drawings which have already been mentioned as contributing largely to a clear understanding in other sections of the book. Thus, the various tracts of the spinal cord and their projections into the brain are not shown in this wise, perhaps because it was felt that such presentation more rightly belongs to a text-book on anatomy.

The well worn cliché, 'This book will find a place on the shelf of every practitioner' does not, of course, apply here. For one thing, German technical prose is not easy to read, even for those who have acquired some conversational facility by their travels; and there are many excellent works on histology in the English language. Still, this is a fine work and the printing, binding and general format make it a very handsome and notable acquisition to one bookshelf in particular.

C.K.O'M.

MECHANISM OF DISEASE

Pathologic Physiology—Mechanisms of Disease: Second Edition. Edited by William A. Sodeman, M.D., F.A.C.P. Pp. xxx + 963. Philadelphia: W. B. Saunders Company. 1956.

Contents: Part I. Pathologic Physiology. Chapter 1. Pathologic Physiology by William A. Sodeman. Part II. Genetics, Growth and Neoplasia. Chapter 2. Genetics of Abnormal Growth and Neoplasma by Madge T. Macklin. Part III. Metabolism and the Endocrine Glands. Chapter 3. Nutritional Factors; Protein and Fat Metabolism by W. A. Sodeman. Chapter 4. Carbohydrate Metabolism by Henry T. Ricketts and James M. Goldinger. Chapter 5. Water and Electrolyte Balance by Roscoe L. Pullen and Robert F. Rushmer. Chapter 6. Endocrine Glands by Edward C. Reifenstein, Jr. Part IV. Infection and Allergy. Chapter 7. Factors Affecting Infections by George T. Harrell, Jr. Chapter 8. Effects of Infection by George T. Harrell, Jr. Chapter 9. Recovery from Infection by George T. Harrell, Jr. Chapter 10. Alteration of the Course of an Infection by George T. Harrell, Jr. Chapter 11. Allergy by Robert A. Cooke and William B. Sherman. Part V. Physical, Toxic and Chemical Agents. Chapter 12. Physical and Toxic Agents by William Bean. Chapter 13. Chemical Agents and Disease by John H. Foulger. Part VI. Circulatory System. Chapter 14. Hemodynamics: The Blood Vessels by W. A. Sodeman. Chapter 15. Dynamics and Circulation of Heart Muscle; Cardiac Reserve; Heart Pain; The Cardiac Cycle by J. T. Roberts. Chapter 16. The Electrocardiogram by F. D. Johnston. Chapter 17. Cardiac Output; Hypertrophy and Dilatation; Valvular Diseases; Congenital Defects; Pericardial Diseases; Extracardiac Factors by Edgar Hull. Chapter 18. Cardiac Failure and Function Tests by John S. la Due. Part VII. Respiratory System. Chapter 19. Pulmonary Ventilation and Respiration; Tests of Respiratory Function by John H. Seabury. Chapter 20. Protective Mechanisms of the Lungs; Pulmonary Disease; Pleural Disease by Harry L. Alexander. Chapter 21. The Esophagus by Walter L. Palmer and Joseph B. Kirsner. Chapter 22. The Stomach by Walter L. Palmer and Joseph B. Kirsner. Chapter 23. The Small Intestine by Leon Schiff. Chapter 24. The Large Intestine by Leon Schiff Chapter 25. The Liver by Franz J. Ingelfinger. Chapter 26. The Gallbladder and Pancreas by Robert Elman. Part IX. Urinary Tract. Chapter 27. The Kidney by A. C. Corcoran and Irvine H. Page. Part X. Blood and Spleen. Chapter 28. Disorders of the Blood by William B. Castle. Chapter 29. The Spleen and Reticuloendothelial System by Charles A. Doan. Part XI. Locomotor System. Chapter 30. The Joints by Richard H. Freyberg. Part XII. Nervous System. Chapter 31. The Nervous System by Russel N. de Jong. Index.

This massive volume of nearly 1,000 pages indicates the trend of medical advance in the last 20 years or so, for the authors are practically all physicians, and include no pathologist or chemical pathologist and but one physiologist. In a book with multiple authorship some unevenness in treatment is to be expected, and in general those subjects in which the major recent advances have been made by physicians and workers in experimental medicine are very well done indeed. The section on disorders of the blood is over 100 pages long, and is a particularly well-balanced up-to-date presentation, and the same could be said of the large and detailed sections on the heart and the kidneys. Neoplasms, however, are discussed only from the point of view of genetics, and while no undue claims are made about the importance of this in man, the presentation is inevitably an unbalanced one. The section on endocrines is surprisingly superficial for a book of this type and most will fail to recognize the Stein-Leventhal syndrome as here depicted. The illustrations are mainly diagrams and, while most are clear and helpful, a few reach heights of misguided ingenuity like the one on the pathological physiology of the spleen.

In a book as large as this it is all too easy to find statements and views open to disagreement, but we cannot refrain from

commenting on the chapter on defence mechanism of the lungs, which falls far below the standards of the rest of the work. The author is of the opinion that bronchioles are lined by epithelium of squamous type, that tubercles largely consist of bacteria in varying stages of viability and mononuclear phagocytes, and that the signs and symptoms of ordinary pulmonary infarcts are due to the fact that most emboli are infected. This section is so bad as to be comic and has little to do with the title of the chapter or with physiology or pathology.

No doubt however this book will be consulted mainly by young physicians, and they will be able to sift the small amount of chaff mainly in two chapters from the abundant grain. For them it can be strongly recommended as a good handbook of modern scientific medicine.

J.G.T.

TREATMENT OF POLIOMYELITIS IN COPENHAGEN

Management of Life-threatening Poliomyelitis, Copenhagen, 1952-1956. With a Survey of Autopsy Findings in 115 Cases. Edited by H. C. A. Lassen, M.D. Pp. xi + 179. 55 Figures. 22s. 6d. net plus 10d. Postage Abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1956.

Contents: Preface. Introductory Remarks. I. Survey of the Epidemic. II. Classification of 345 Cases of Life-threatening Poliomyelitis. III. The Anaesthetist and Positive Pressure Breathing. IV. Therapeutic Indications. V. Basic Mechanics of Artificial Ventilation. VI. The Acute Stage: Clinical Observation. VII. The Acute Stage: Tracheotomy and Bronchoscopy. VIII. The Acute Stage: Artificial Ventilation. IX. The Acute Stage: Lung Physiotherapy. X. The Acute Stage: Complications and Special Conditions. XI. Convalescent and Chronic Stage: Course of Respiratory Paralysis. XII. Convalescent and Chronic Stage: Decannulation and Late Complications in Tracheotomy. XIII. Convalescent and Chronic Stage: Weaning Problems in Artificial Ventilation. XIV Laboratory Control of Gas Exchange. XV. Laboratory Findings. XVI. Electrocardiographic Changes in Acute Poliomyelitis. XVII. Renal Calculi and Artificial Ventilation. XVIII. Results. XIX. Autopsy Findings. References. Index.

In 1952 Copenhagen had a formidable polio epidemic. It surpassed all other previous experience of that city not only by its size but even more by the high evidence of cases needing attention to the respiratory system. The author puts this unclearly by speaking of these cases as suffering from 'involvement of the upper part of the nervous system'. From August to the end of the year 3,000 patients with a diagnosis of poliomyelitis were admitted to the Bleedam Hospital, where the writer is chief physician for communicable diseases. (He is also professor of epidemiology of the University of Copenhagen.) In 2,241 the diagnosis was confirmed. Of a total of about 1,250 cases with paralysis no less than 345 had 'insufficiency of respiration or impairment of swallowing or both'. The author says rightly that the treatment of bulbar and respiratory poliomyelitis is one of the most difficult problems in medical management. He wisely called in the anaesthetist, who then participated in the team treating these cases.

This book deals mainly with this aspect of treatment. He discusses the various apparatus in current use and everyone will agree with him as regards their serious defects. Most institutions have come to look upon the cuffed tracheotomy tube as the most satisfactory method available, used with positive oxygen-pressure. The author goes into this fully and speaks from considerable experience. The book should be consulted for the details of this method; they need careful attention.

The indications for tracheotomy are much broader than we are accustomed to. The term respiratory failure used in this book is given a very comprehensive meaning and explains the high figure of 345 respiratory cases. We are surprised to find very little said of diaphragmatic and intercostal paralysis—the usually accepted indications for these special methods of treatment. We know that an ever-present danger even in non-respiratory neurological cases (not necessarily polio) is the tendency to develop pneumonia. This in turn causes worsening of the neurological state, apart from its own inherent risk—an aspect particularly important in polio, in which so much of the disease is reversible. The author may be right in advocating tracheotomy for patients without any respiratory paralysis in whom the breathing is merely depressed as the result of mental dulling—these patients, when asked to breathe deeply, promptly respond—there is no paralysis or paresis. But we have no figures for comparison. These are the cases we need to get to know most about. Tracheotomy is not a trifling procedure.

Respiratory and swallowing disturbances are not the only ones discussed. Acute pulmonary oedema, paralytic ileus, shock, uraemia, etc., are briefly dealt with.

The author defines hyperpyrexia as 'a body-temperature of at least 102·2°F until death or consecutively for the first 5 days after admission. By this definition we have tried to exclude cases of hyperpyrexia due to secondary infection'. This and a few other statements of minor import can hardly be accepted. But the main purpose of the book needs serious consideration.

F.F.

AFRICAN MEDICINE AND MAGIC

Medicine and Magic of the Mashona. By Michael Gelfand, O.B.E., M.D., F.R.C.P. Pp. 266. 35 Plates. 25 Drawings. 25s. Cape Town, Wynberg, Johannesburg: Juta and Company Limited. 1956.

Contents: I. The Tribal Mhondoro. II. The Family Mhondoro. III. Mudzimu: Ancestral Spirit. IV. Muroi: Witch. V. Ngozi Aggrieved Spirit. VI. Shave: Alien Spirit. VII. Nganga: The Doctor. VIII. The Clothes and Equipment of the Nganga. IX. The Approach to the Nganga. X. Hakata. The 'Bones'. XI. Preventive Medicine. XII. The Herbalist and his Remedies. XIII. Pregnancy (Nhumbu or Mimba). XIV. Death. Bibliography. Glossary. Index.

In a foreword Sir Robert Tredgold says these appropriate words concerning Dr. Gelfand: 'A highly trained scientist who is yet prepared to study with sympathy and without arrogance the strivings of those who, in a far more elementary way are seeking, like him, to find an answer to the great mysteries of life and death . . . he has the understanding heart. His own sincerity and genuine interest has evoked a confidence that is not lightly given'. He adds: 'This book ought to help towards a better understanding of the African mind'.

The European thinks of the African as a care-free, smiling, happy individual, and has asked himself the question time and again whether the Native is not happier than civilized man. The reader of this book will wonder whether behind the happy-go-lucky exterior there are not perpetual fears which harrass the African. Is his life full of anxieties about the numerous and varied spirits ready to plague him, often through no fault of his own? True, he can have recourse to the *nganga* (witch-doctor), but by this time there may have been serious illness or death, loss of crops or cattle. How much is he preoccupied with these fears? The book does not deal with this aspect of Native life. We hope Dr. Gelfand, who has written a good deal on African sickness and on African medicine and practice, will write on this too.

The Shona believe that sickness is caused by spirits—ancestral spirits and alien spirits; there are also the spells and poisons of witches. Until the cause of the illness (in this sense) is recognized by the family little can be done to cure the patient or ward off death or prevent other members of the family from being affected. They turn to the *nganga* because he can contact the spirit world and find out what is necessary to propitiate the spirits. Amongst the Africans there are a variety of types and grades of *nganga*, distinct specialists. There are two large groups, the diviner (diagnostician) and the herbalist (therapeutist), though most of them combine both arts to a greater or lesser degree. There is a tradition of handing on the profession from father to son, and occasionally daughter.

Dr. Gelfand says that in his experience amongst the Africans no *nganga* demonstrated any attempt at surgery, though he has read that elsewhere in Africa major operations are performed by primitive medicine-men. Nor has he seen a splint used for a broken limb, but he has heard mention of it by some observers. The tourniquet is used. And so is cupping.

It is very interesting to observe how divergent the regional treatment so frequently is for the same illness or the same cause. The reviewer has heard from Dr. Gelfand himself that the African does not dare touch a patient in an epileptic fit. If the subject falls into the fire (he often does, as can be expected from the Native habit of sitting round fires) his relatives and friends leave him as he falls. Consequently bad burns are commonly seen in the Rhodesian hospitals. It is to be noticed that no antispasmodic drugs are used for asthma—which is strange.

Dr. Gelfand has written a most interesting book.

F.F.